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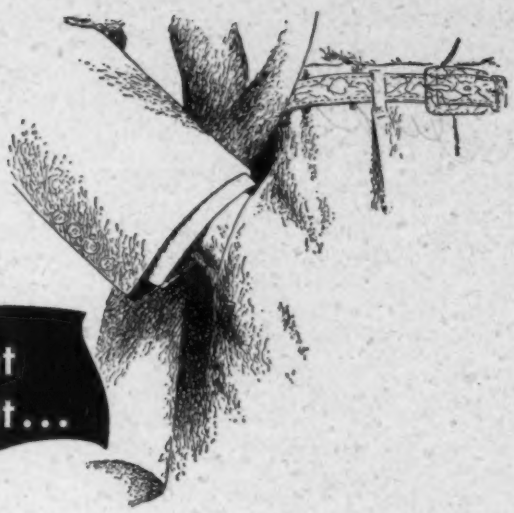

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Original Communications

COMBINED IMMUNIZATION AGAINST DIPHTHERIA, TETANUS, AND PERTUSSIS IN CHILDREN OVER THREE MONTHS OF AGE; INCLUDING AN EVALUATION OF THE EFFECTIVENESS OF TWO IMMUNIZING AGENTS

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SIMULTANEOUS injection of three or more antigens has been advocated by Ramon[1] for a number of years. In this country Lapin[2, 3] and Daughtry-Denmark[4] were the first to use combined immunization against diphtheria, tetanus, and pertussis. Since then, "triple combined immunization" has come into general use, and a number of commercial preparations are now available.

The object of this investigation is to evaluate the effectiveness of two immunizing agents by serial titrations of the serum levels of tetanus and diphtheria antitoxin and of serum agglutinins for *Hemophilus pertussis*. It is further desired to compare the incidence and severity of reactions to injections of these two immunizing agents.

The two preparations* used were: (1) fluid diphtheria and tetanus toxoids with 40 billion *H. pertussis* added per cubic centimeter,† and (2) aluminum hydroxide-adsorbed diphtheria and tetanus toxoids with 20 billion *H. pertussis* added per cubic centimeter.‡ Miller has previously reported on the use of alhydrox.[5]

PLAN OF THE EXPERIMENT

The children included in the investigation were divided into two groups as alike as possible in age, sex, and color. To one group, *Series A*, plain DPT vaccine was given; the other group, *Series B*, received alhydrox. The age distribution is shown in Fig. 1. In the "A" series there were sixty-three females and fifty-five males; in the "B" series, fifty-two females and fifty-three males. In Series A there were seventy-six white and forty-two Negro children; in Series B there were fifty-six white, forty-eight Negro and one Chinese.

From Babies Hospital, Vanderbilt Clinic, and the Department of Pediatrics, Columbia University.

Supported by a grant from Cutter Laboratories, Berkeley, Calif.

*Kindly supplied by Cutter Laboratories, Berkeley, Calif.

†Referred to hereafter as "plain DPT vaccine."

‡Referred to hereafter as "alhydrox."

The immunization schedule for the two series is detailed in Table I. In the "A" series, immunization of fifty-seven children was started with an injection of 0.1 c.c. of plain DPT vaccine, followed one week later by the injection of 0.5 c.c. that initiated the regular series. This precaution was taken at the beginning of the investigation to avoid severe reactions to the vaccine. Only thirty-seven of the fifty-seven patients were tested for serum antibody titer. Because of the small dose given, the short interval between the first two injections, and the lack of increased antibody response, as compared with the other cases receiving an initial dose of 0.5 c.c., it is felt that this additional 0.1 c.c. of vaccine can be disregarded safely in evaluating the results.

TABLE I. SCHEDULE OF IMMUNIZATIONS

INJECTIONS	PLAIN DPT VACCINE (40 BILLION H. PERTUSSIS PER C.C.) (C.C.)	ALHYDROX (20 BILLION H. PERTUSSIS PER C.C.) (C.C.)
1st injection	0.5	0.5
2nd injection (1 month after first)	1.0	1.0
3rd injection (1 month after second)	1.0	1.0
Total dose *H. pertussis*	100 billion	50 billion

Blood samples for agglutinin and antitoxin determinations were obtained as follows: (a) before immunization; (b) about one month (one to two months) after completion of the immunization series: and (c) about six months (six to nine months) after completion of the immunization series. Schick tests were done in twenty-four children of series A and in thirteen of series B after the second postimmunization blood sample had been obtained.

LABORATORY METHODS

The diphtheria antitoxin titrations were carried out in guinea pigs according to a modification of the Kellog test.

The titrations of tetanus antitoxin were done according to the method recommended by the National Institute of Health.

The serum agglutinins against *H. pertussis* were determined by the Cutter modification of the method of Miller[6] and by the method of Flosdorf.[7] A fresh antigen was also used in performing the agglutinative tests after this date.

All laboratory determinations were done by the Biological Control Division of Cutter Laboratories, Berkeley, Calif. The blood samples obtained were labeled according to a code system* known to the group carrying out the clinical part of the investigation, but unknown to the people doing the laboratory determinations. The samples were numbered progressively as obtained and in the same code were included not only children of the two series here reported, but also those of three other groups to be reported at a later date. This precaution provided a further check of the antibody and antitoxin titrations.*

*Not included in this code system were most of the preimmunization blood samples of both series and forty of the specimens obtained one month after immunization in Series A.

AGGLUTININ AND ANTITOXIN LEVELS CONSIDERED PROTECTIVE

An agglutinin titer of 1:320 against *H. pertussis* has been considered in this study as a satisfactory immune antibody level. It has been shown by Miller[8] and more recently by Sako,[9] that 100 per cent of patients having this titer or more of serum agglutinins have clinical protection against intimate exposure to whooping cough. Hereafter, children having a titer of 1:320 or more will be referred to as having a protective level of antibodies. Those having less than this level of serum agglutinins will be considered as not having a titer sufficient for protection against pertussis.

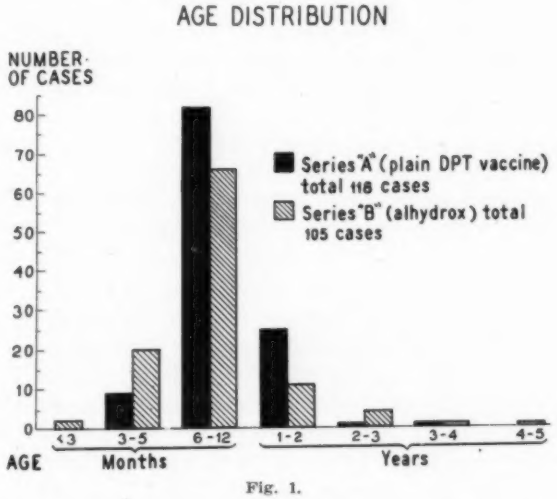

Fig. 1.

A level of 0.03 unit or more of diphtheria antitoxin per cubic centimeter was considered as affording complete protection to the individual. Titrations were not carried out below this level. It should be noted that the minimum level tested for is in reality seven and a half times as great as the 0.004 units per cubic centimeter generally accepted as sufficient to induce Schick negativity in the average individual.[10]

In the case of tetanus antitoxin the minimum level tested for was 0.01 unit per cubic centimeter. A titer of 0.1 unit per cubic centimeter has been generally considered protective against infection by *Clostridium tetani*.[6, 11]

LOCAL AND GENERAL REACTIONS TO IMMUNIZATION

In Table II are tabulated the local and general reactions to 635 injections in the two series of cases. Almost no severe local reactions were observed. From 0 to 10 per cent of cases in the various groups experienced temperatures of more than 102° F. In no case did the temperature go above 104° F. The "high fevers" generally ranged between 102° and 103° F. In one instance the

TABLE II. REACTIONS

VACCINE	INJECTION	TOTAL NO. INJECTIONS	LOCAL REACTIONS: ERYTHEMA (CM.) 0 (%)	<2.5 (%)	2.5–5 (%)	>5 (%)	INFILTRATION (CM.) 0 (%)	<2.5 (%)	2.5–5 (%)	>5 (%)	FEVER (%) NONE	SLIGHT (100°-102° F.)	HIGH (102°-104° F.)	OTHER REACTIONS (%) IRRITABILITY	VOMITING	ANOREXIA
Series A, plain DPT vaccine	A 0.1 c.c.	57	42	43	15	0	44	42	14	0	77	23	0	19	0	0
	1st 0.5 c.c.	107	46	39	15	0	48	40	12	0	72	21	7	24	3	6
	2nd 1.0 c.c.	97	76	20	4	0	76	20	4	0	81	12	7	19	1	4
	3rd 1.0 c.c.	85	86	13	1	0	85	14	1	0	91	7	2	5	0	1
Series B, alhydrox	1st 0.5 c.c.	105	48	37	14	1	43	41	15	1	67	24	9	22	5	7
	2nd 1.0 c.c.	96	63	27	10	0	53	37	10	0	65	25	10	25	7	4
	3rd 1.0 c.c.	88	63	37	0	0	58	41	1	0	79	13	8	11	6	1

second injection of "alhydrox" was followed by a temperature of 104° F. and convulsions. This child, a Negro boy 2 years of age, was admitted to Babies Hospital. Examination of the spinal fluid was entirely negative, the fever subsided within twenty-four hours, and the patient was discharged in good health the day after admission. A subsequent injection of the same material failed to produce a febrile response. It was felt that the child reacted to the high temperature with convulsions and that this response of the central nervous system could not be attributed directly to the inoculation of vaccine. It might be added that the febrile reactions usually appeared at about twelve to twenty-fours hours after injection and lasted an average of twelve to twenty-four hours.

In all patients, erythema and induration usually became apparent at the site of injection within twelve to twenty-four hours and lasted an average of forty-eight hours. In the majority of subjects receiving alhydrox, a small, deep, nonpainful nodule was palpable at the site of inoculation for several weeks. There were no abscesses, sterile or otherwise, requiring drainage; but in one instance after the third injection of alhydrox, a fluctuating area of probable necrosis appeared at the site of injection. This area eventually disappeared without drainage. Nine patients of Series A and six of Series B complained of "sore arms," even though other signs of local inflammation were not especially severe.

Among the reactions other than those just described, irritability, vomiting, and anorexia were the most common. In three instances there was a complaint of mild diarrhea after an injection of vaccine. This may well have been coincidental. In one case generalized hives developed the day after injection, but this manifestation responded readily to an injection of adrenalin.

Several interesting observations can be made from an analysis of Table II:

1. There was very little difference between the two series of cases in the percentage of reactions.

2. The type and intensity of the local reactions did not depend on the amount of vaccine given. In Series A, fifty-seven patients were given a first injection of 0.1 c.c. of the plain DPT vaccine (designated "injection A" in Table II); no significant difference could be seen in the number and type of local reactions to this small dose as compared with other larger injections.

3. The number and severity of the reactions decreased in both series with subsequent injections.

Inspection of the data also reveals that reactions in a single case are entirely unpredictable. It is not possible to predict the response to an injection of vaccine on the basis of previous experience in the same child. The cases in this study were selected only as to age, hence several children with allergic manifestations were included. We are not aware of a difference in response to inoculation between this group and nonallergic children, a fact which is in accord with statements made by other observers.[11]

Finally, it should be mentioned that no effort was made to direct the needle downward, in giving the injection, as recommended by Sauer.[12] The vaccine was inoculated deep subcutaneously or intramuscularly, attention being paid to the avoidance of introduction of vaccine in the skin when passing through it, as suggested by Sako.[13]

RESULTS OF AGGLUTINATION TESTS FOR H. PERTUSSIS

1. *Series A.*—The results of the agglutinative tests for *H. pertussis* before and after immunization with plain DPT vaccine are shown in Table III. It will be noted that of the thirty-three children tested before immunization, eight (24.3 per cent) had agglutinin titers of more than 1:320. In fact, if one includes cases with titers lower than this, more than 50 per cent of the children tested had agglutinins against *H. pertussis.* This figure is not in agreement with the results of most investigators,[6, 9] although it corresponds to the findings of others.[14] This subject will be discussed in more detail later in this paper.

TABLE III. SERIES "A" (PLAIN DPT VACCINE) TITRATION OF SERUM AGGLUTININS AGAINST HEMOPHILUS PERTUSSIS

AGGLUTININ TITERS	NO. CASES		
	BEFORE IMMUNIZATION	1 MONTH AFTER IMMUNIZATION	6 MONTHS AFTER IMMUNIZATION
1:0	15 (45.4%)	7 (8.1%)	9 (13.0%)
1:50	5	1	2
1:100	1	1	1
1:200	4	3	3
Total cases without a protective titer	25 (75.7%)	12 (14.0%)	15 (21.7%)
1:400	1	9	7
1:800	2	7	6
1:1600	4	18	12
1:3200	1	40 (46.5%)	29 (42.0%)
Total cases with a protective titer	8 (24.3%)	74 (86.0%)	54 (78.3%)
Total cases in each group	33	86	69

One month after completion of the course of injections, 86 per cent of the children tested had an agglutinin titer of more than 1:320, a level which is believed to afford complete protection. Almost half of the group tested (46.5 per cent) had agglutinins in the very high titer of 1:3,200 or more. While susceptibility is not present in the presence of agglutinins in high titer, 1:320 or more, immunity may exist in the absence of agglutinins [8, 9] and a substantial number of subjects with low agglutinin titers are found to be immune when exposed to whooping cough. Since some of the children with low or no agglutinin titers are therefore not susceptible to infection, this may be estimated to bring the total protected to approximately 90 per cent, which is the maximum obtainable with any type of vaccination.[5] The results obtained in the vaccination of this series of children should, therefore, be considered satisfactory.

If the agglutinin titers obtained at one month and six months after completion of immunization are compared, it will be seen that there has been no significant drop in the five-month period. Indeed, if figures for the total number of patients with a protective titer at one month and six months after immunization are analyzed statistically, it is found that the variation in the figures may be readily accounted for by chance alone ($\chi^2 = 0.9179$, P = .35). The same is true of the patients with a titer of 1:3,200 or more ($\chi^2 = 0.0478$, P = 0.85).

2. *Series B.*—The serum agglutinin titers obtained before and after immunization with alhydrox are given in detail in Table IV. Remarks made about preimmunization titers in children of Series A apply also to the subjects in this group.

TABLE IV. SERIES B (ALHYDROX) TITRATION OF SERUM AGGLUTININS AGAINST HEMOPHILUS PERTUSSIS

AGGLUTININ TITERS	NO. CASES		
	BEFORE IMMUNIZATION	1 MONTH AFTER IMMUNIZATION	6 MONTHS AFTER IMMUNIZATION
1:0	40 (48.2%)	4 (4.8%)	10 (12.5%)
1:50	13	2	0
1:100	6	2	1
1:200	12	4	3
Total cases without a protective titer	71 (86.6%)	12 (14.6%)	14 (17.5%)
1:400	3	9	4
1:800	3	8	10
1:1600	3	22	15
1:3200	2	31 (37.8%)	37 (46.2%)
Total cases with a protective titer	11 (13.4%)	70 (85.4%)	66 (82.5%)
Total cases in each group	82	82	80

One and six months after immunization, more than 80 per cent of the children tested had a titer of more than 1:320, about 40 per cent a titer of 1:3,200 or more. Inspection alone reveals that at the end of the two periods of time there is no difference between the total numbers of cases showing a titer of more than 1:320. Analysis by statistical methods reveals that the difference between the numbers of children with a titer of 1:3,200 or more is more apparent than real and can be accounted for by sampling error ($\chi^2 = 1.442$, P = 0.25). The remarks made about the total number of children presumably protected after immunization apply equally to this group of patients.

3. *Comparison between Series A and B.*—If the data in Tables III and IV are analyzed, it will be seen first that the results of the agglutinative tests *before immunization* are directly comparable in the two series. While the number of children tested is greater in Series B, the proportion of cases showing the presence of agglutinins is a little over 50 per cent in each series. The number of children with preimmunization titers of 1:320 or more is also not significantly different ($\chi^2 = 0.972$, P = 0.40).

In comparing the two series, analysis of the agglutinative titers obtained one month and six months after immunization shows that there is no significant difference between the numbers of cases with a titer of 1:320 or more. The same can be said about children with titers of 1:3,200 or more.

In conclusion, the results of immunization against pertussis are equally satisfactory in both series, as proved by the percentage of titers of 1:320 or more. In view of the fact that half the dose of *H. pertussis* was administered in the immunization with "alhydrox" as compared with plain DPT vaccine (see Table I), we must conclude, on the basis of our results, that the former is superior to the latter as an immunizing agent against *H. pertussis*. Moreover, it should be pointed out that the total dose of 50 billion organisms used in our "B" series is below the minimal amount advocated by other authors.[3, 11]

RESULTS OF TITRATION OF DIPHTHERIA ANTITOXIN

1. *Series A.*—The results of titrations of diphtheria antitoxin before and after immunization with plain DPT vaccine are shown in Table V. Of the thirty-three patients tested before immunizaton, only three had a titer of 0.03 unit per cubic centimeter or more. It should be kept in mind, however, that 0.03 unit, the minimum titer tested for, is much more than is needed to produce Schick negativity. In all probability, therefore, a larger number of children than indicated by our figures were Schick negative before immunization. Schick tests were not carried out at this time, lest the injection of skin test material act as an antigen and thus confuse the interpretation of the experimental vaccination.

TABLE V. SERIES "A" (PLAIN DPT VACCINE) TITRATION OF DIPHTHERIA ANTITOXIN

ANTITOXIN LEVELS (UNITS PER C.C.)	NO. CASES		
	BEFORE IMMUNIZATION	1 MONTH AFTER IMMUNIZATION	6 MONTHS AFTER IMMUNIZATION
Total patients without a protective titer (<0.03 unit per c.c.)	31 (90.9%)	0	9 (13.0%)
0.03	–	1	–
>0.03 <0.1	1	–	6
0.1	1	5	1
>0.1 <1.0	–	19	17
1.0	–	10	12
>1.0	–	51 (59.3%)	24 (34.7%)
Total cases with a protective titer	3 (9.1%)	86 (100%)	60 (87.0%)
Total cases in each group	33	86	69

One month after completion of the course of injections all cases tested had an antitoxin level of 0.03 unit or more, and fifty-one (59.3 per cent) out of a total of eighty-six a high titer of more than 1.0 unit per cubic centimeter. The results of vaccination against diphtheria with plain DPT vaccine are to be considered highly satisfactory.

Five months later, six months after completion of the immunization, the proportion of cases with a titer of 0.03 units or more had dropped from 100 to 87 per cent, a difference which is to be considered highly significant and not due

to chance in sampling ($\chi^2 = 9.643$, $P = <0.01$). There was also a drop in the number of children with a titer of more than 1.0 units per cubic centimeter, which, while statistically less impressive, is, nevertheless, within the limits of significance ($\chi^2 = 4.861$, $P = 0.03$). A drop in titer is expected, for it is known that the diphtheria antitoxin content in blood of immunized subjects slowly decreases with the passage of time.[15]

Three of the nine children found at this time to have antitoxin levels of less than 0.03 unit per cubic centimeter were Schick tested shortly afterward, and all had negative tests. Among twenty-one subjects whose serum antitoxin titer was 0.03 unit or more per cubic centimeter six months after the completion of their immunizing course, Schick tests were uniformly negative, as was to be expected.

2. *Series B.*—The levels of diphtheria antitoxin obtained before and after immunization with alhydrox are detailed in Table VI. Of eighty-three children tested before immunization, sixteen (18.3 per cent) had antitoxin titers of 0.03 unit per cubic centimeter or more. A greater number, undoubtedly, were Schick negative, but skin tests were withheld at this time for reasons already given. The results of immunization, as can be seen, were highly satisfactory both one month and six months after completion of immunization. One child, who had failed to develop a titer of 0.03 unit per cubic centimeter of antitoxin one month after immunization, had developed a level of more than 1.0 unit per cubic centimeter when retested five months later.

While there was no difference at one month and six months postimmunization in the total number of patients showing protective levels, there was a drop in the number of those with an antitoxin level of more than 1.0 unit per cubic centimeter from 84 to 41 per cent. If these figures are analyzed, the difference is found to be highly significant and due to some factor other than chance ($\chi^2 = 31.598$, $P = «0.01$).

Schick tests carried out on "B" subjects after the six months' postimmunization blood samples had been collected were uniformly negative.

3. *Comparison Between Series A and B.*—If Tables V and VI are compared, it will be noted that in Series B there was a greater percentage of children with protective titers before immunization. While this difference is not great and could be due to chance alone ($\chi^2 = 2.522$, $P = 0.12$), it can be explained readily by the higher percentage of children below 6 months of age in Series B (Fig. 1).

Analysis of data obtained one month postimmunization reveals no real difference between the percentage of patients with a protective titer in the two series. Six months after immunization, the percentage of children in *Series B* showing protective levels of antitoxin is significantly higher than in Series A ($\chi^2 = 8.926$, $P = <0.01$).

At one month after immunization, the percentage of "B" patients with an antitoxin level of more than 1.0 unit per cubic centimeter is significantly higher than of the "A" cases. But five months later there is no significant difference between the two groups ($\chi^2 = 0.0006$, $P = 0.98$), a sharper decline having occurred in the high titers in the "B" series.

TABLE VI. SERIES B (ALHYDROX) TITRATION OF DIPHTHERIA ANTITOXIN

ANTITOXIN LEVELS (UNITS PER C.C.)	NO. CASES		
	BEFORE IMMUNIZATION	1 MONTH AFTER IMMUNIZATION	6 MONTHS AFTER IMMUNIZATION
Total cases without a protective titer (<0.03 unit per c.c.)	67 (81.7%)	1 (1.5%)	0
0.03	8	–	1
>0.03 <0.1	4	1	5
0.1	2	1	1
>0.1 <1.0	1	4	27
1.0	–	6	13
>1.0	–	69 (84.1%)	33 (41.2%)
Total cases with a protective titer	15 (18.3%)	81 (98.5%)	80 (100%)
Total cases in each group	82	82	80

TABLE VII. SERIES A (PLAIN DPT VACCINE) TITRATION OF TETANUS ANTITOXIN

ANTITOXIN LEVELS (UNITS PER C.C.)	NO. CASES		
	BEFORE IMMUNIZATION	1 MONTH AFTER IMMUNIZATION	6 MONTHS AFTER IMMUNIZATION
<0.01	32	0	0
>0.01 <0.1	1	0	0
Total cases without a protective titer (<0.1 unit per c.c.)	33 (100%)	0	0
0.1	–	–	1
>0.1 <1.0	–	2	7
1.0	–	3	8
>1.0	–	81 (94.1%)	53 (76.8%)
Total cases with a protective titer	0	86 (100%)	69 (100%)
Total cases in each group	33	86	69

The results of immunization against diphtheria are satisfactory in both groups. As we have pointed out, six months after immunization there was no decline in the total number of children with protective titers in the "B" series as compared with a clear-cut drop in the "A" series. On this basis, one might say that alhydrox is a better immunizing agent against diphtheria than the plain DPT vaccine. On the other hand, as we have said, the number of cases with a titer of more than 1.0 unit per cubic centimeter decreased much more markedly in the "B" series than in the "A" series in the five-month interval between testing. This finding makes one suspect that, in the long run, the results with both immunizing agents would even out eventually and thus be closely comparable.

RESULTS OF TITRATION OF TETANUS ANTITOXIN

1. *Series A.*—The levels of tetanus antitoxin in the serum of children before and after immunization with plain DPT vaccine are tabulated in Table VII. Before immunization, all children tested had titers below the protective level. This is as expected, for tetanus antitoxin does not occur normally in the blood of human beings.[15]

After immunization, all patients showed antitoxin levels above the protective level, and the majority showed a high titer of more than 1.0 unit per cubic centimeter. The drop in the number of children with high titers in the interval between one and six months after immunization is statistically significant ($\chi^2 = 8.439$, $P = <0.01$). This is to be expected, for it is known that the levels of tetanus antitoxin decrease gradually with the passage of time.[15]

2. *Series B.*—The levels of tetanus antitoxin before and after immunization with alhydrox are detailed in Table VIII. None of the children tested before immunization had protective levels of tetanus antitoxin, while 100 per cent produced levels of more than 0.1 unit per cubic centimeter after immunization. Especially interesting is the high level of antitoxin in more than 90 per cent of the subjects at both one and six months after immunization.

TABLE VIII. SERIES B (ALHYDROX) TITRATION OF TETANUS ANTITOXIN

ANTITOXIN LEVELS (UNITS PER C.C.)	NO. CASES		
	BEFORE IMMUNIZATION	1 MONTH AFTER IMMUNIZATION	6 MONTHS AFTER IMMUNIZATION
<0.01	82	0	0
>0.01 <0.1	0	0	0
Total cases without a protective titer (<0.1 unit per c.c.)	82 (100%)	0	0
0.1	–	–	1
>0.1 <1.0	–	3	1
1.0	–	1	5
>1.0	–	78 (95.1%)	73 (91.2%)
Total cases with a protective titer	0	82 (100%)	80 (100%)
Total cases in each group	82	82	80

3. *Comparison of Series A and B.*—When the data in Tables VII and VIII are compared, it will be seen that the results of immunization against tetanus are satisfactory in both series. While in Series A the number of children with a titer of more than 1.0 unit per cubic centimeter dropped from 94 per cent one month after immunization to 77 per cent five months later, there was no change in the number of cases with a titer of 1.0 unit per cubic centimeter in the "B" series. On the basis of this fact it must be concluded that alhydrox is a better immunizing agent against tetanus than the plain DPT vaccine.

DISCUSSION

1. *Patients With "Protective" Agglutinin Titers Against H. pertussis Before Immunization.*—The most controversial feature of the findings we have described in this paper is the high percentage of children showing agglutinative titers against *H. pertussis* before immunization. In a report made by Miller[6] the proportion of patients showing agglutinins before immunization was 10 per cent, and in no case was the titer more than 1:160. In Sako's recent paper[9] it is stated that the pre-immunization agglutinative tests were negative in all of the 8,600 children included in his investigation. In a recent paper of DeGara and Mayer[16] only one out of seventeen children showed the presence of agglu-

tinins before immunization. Adams and Kimball[17] of Minneapolis found that 23 per cent of the cord bloods they tested showed the presence of agglutinins in titers of 1:20 to 1:180.

Two facts stand out from this brief and admittedly incomplete review of the literature: there is a lack of sufficient data on pre-immunization agglutinative titers in the literature, and there is considerable disagreement among the findings of various authors. This leads one to believe that there is either a difference in the rate of exposure to pertussis in different parts of the United States or that the agglutination tests do not give consistent results in the hands of different laboratories. Probably both factors are involved.

It must be admitted, however, that in our two series the frequency of subjects showing the presence of agglutinins before immunization exceeds that of most other reports. Only Waddel and L'Engle[14] have had a comparable experience: 73 per cent of their twenty-two cases tested at one week of age had agglutinins in the serum. Of the twenty-two cases, eight (37 per cent) had titers of more than 1:320. As the titrations of agglutinins in their study were also done by the Cutter Laboratories, it is reasonable to suspect that the pre-immunization results obtained in our cases by the Cutter modification of the Miller technique were too high. This suspicion is borne out by the fact that subsequent titrations, carried out by the same laboratory according to the method of Flosdorf and (what is probably more important) with a fresh antigen, showed the absence of pre-immunization agglutinative titers in almost all of a group of newborn infants tested.[18]

It might be reasonably assumed that children of more than 6 months of age showing the presence of agglutinins before immunization had been previously exposed to *H. pertussis* or some of its antigens. An analysis of the cases with pre-immunization titers reveals, however, that the number of such children that responded to immunization with a high agglutinin titer (more than 1:1,600) does not differ significantly from the percentage of children with high post-immunization titers found for the whole series. No conclusion can be drawn as to the rate of exposure of subjects with pre-immunization agglutinin titers.

In eight cases the agglutinative titer present before immunization decreased on subsequent examination. In two instances, the infants 6½ and 7½ months of age, the titers were found to have decreased progressively from those before immunization at each examination so as to reach a titer of 1:0 six months after completion of the immunizing series. In both of these cases the presumption that the initial titer was due to passive transfer of antibodies from the mother to the child is strongly founded. In a third case, only 6 weeks of age, the same conclusion can apply. In the remaining five cases the presence of agglutinins before immunization is more difficult to explain and the possibility of self-agglutinating cultures must be considered.

2. *Patients with "Protective" Agglutinative Titers Against H. pertussis After Immunization.*—All of the blood samples obtained six months after immunization in the "B" series and thirty-four of sixty-nine specimens collected at the same time interval in the "A" series were tested for pertussis agglutinins

by the Flosdorf method and with a fresh antigen. As previously pointed out, there was no decline in the agglutinin titers between one and six months after immunization in either series. This leads to the obvious inference that the results of all of the postimmunization agglutinative tests are to be considered reliable. In addition, the agglutinin titers obtained by Miller[5] after immunization with alhydrox checked very closely with ours.

3. *"Poor Immunizers."*—If the cases showing an agglutinative titer of less than 1:320 at either one month or six months after immunization are considered, it is found that in most instances the agglutinin titers were low at both times. In other words, these children were poor producers of agglutinins against *H. pertussis.* It does not follow, as we have previously mentioned, that these same individuals were not immune to pertussis, even though their serum antibody level was low.

In some instances, the same children who did not produce enough agglutinins against pertussis to obtain good serum levels, had an adequate production of diphtheria and tetanus antitoxins. In others (see Table IX) it is clear that the subjects were poor immunizers against more than one antigen.

TABLE IX. PATIENTS WITH POOR RESPONSE TO IMMUNIZATION

	PRE-IMMUNIZATION TITERS			TITERS ONE MONTH POSTIMMUNIZATION			TITERS SIX MONTHS POSTIMMUNIZATION		
CASE*	AGGLUTININS FOR PERTUSSIS	TETANUS ANTITOXIN (UNITS/C.C.)	DIPHTHERIA ANTITOXIN (UNITS/C.C.)	AGGLUTININS FOR PERTUSSIS	TETANUS ANTITOXIN (UNITS/C.C.)	DIPHTHERIA ANTITOXIN (UNITS/C.C.)	AGGLUTININS FOR PERTUSSIS	TETANUS ANTITOXIN (UNITS/C.C.)	DIPHTHERIA ANTITOXIN (UNITS/C.C.)
A75		Not done		1:800	>1.0	1.0	1:200	>0.3 <1.0	<0.03
A90	1:0	<0.1	<0.03	1:0	>1.0	>0.1 <1.0	1:0	>1.0	<0.03
A106	1:0	<0.1	<0.03	1:400	>1.0	>0.1 <1.0	1:0	0.3	<0.03
A108	1:50	<0.1	<0.03	1:3200	>1.0	1.0	1:50	>1.0	<0.03
B98	1:0	<0.1	<0.03	1:0	>1.0	>1.0	1:0	>1.0	0.1

*A, patients in "A" series (plain DPT vaccine).
B, patients in "B" series (alhydrox).

Fluctuation of the agglutinin titers was noted in some cases but, as shown in Tables III and IV, it was not such as to interfere with the interpretation of the results.

4. *Relationship of Systemic Reactions to Agglutinin and Antitoxin Titers.*—Sako[13] states "as a general rule, the more severe the reaction, the higher the titer of agglutinins for H. pertussis." An analysis of the cases in our series that had a moderate or severe systemic reaction (fever of 102° F. or more) fails to corroborate this statement. The agglutinin and antitoxin titers after immunization in these children were not significantly different from those in subjects without systemic reactions.

The number of severe local reactions was too small to permit us to draw any conclusion in this respect.

SUMMARY AND CONCLUSIONS

1. The response of children of more than 3 months of age to combined immunization against diphtheria, tetanus, and pertussis was studied by means of serum agglutinin and antitoxin determinations before and at various intervals after immunization. Two immunizing agents were used: fluid diphtheria and tetanus toxoid with 40 billion *H. pertussis* added per cubic centimeter (plain DPT vaccine) and aluminum hydroxide-absorbed diphtheria and tetanus toxoids with 20 billion *H. pertussis* added per cubic centimeter (alhydrox).

2. In 635 injections of the two immunizing agents, it was found that the systemic and local reactions to the two preparations did not differ significantly. It was noted that the type and intensity of the local reactions did not depend on the size of the injection, but decreased with subsequent inoculations. Constitutional reactions were not severe and no sterile abscesses requiring drainage were observed.

3. The postimmunization titers were satisfactory in both series of cases. It was felt that alhydrox was a better immunizing agent against pertussis than plain DPT vaccine because equally good results were obtained with half the dose of *H. pertussis*. In the case of diphtheria and tetanus, alhydrox was also found to give better results. The antitoxin titers obtained with this agent were higher and more enduring than those observed after injection of the plain DPT vaccine.

4. A review of the literature reveals that there is a dearth of data concerning pre-immunization agglutinative tests and a considerable discrepancy among the results of various authors. The agglutinin titers against *H. pertussis* before immunization in our cases were higher than those of most other reported series. This may have been due to technical factors in the agglutinative tests. When the antigen and the method were later changed, our results conformed more nearly with those reported in the literature.

5. The postimmunization pertussis agglutinative titers are to be considered reliable because most of the blood samples obtained six months after immunization were tested with a fresh antigen.

6. Some instances of "poor immunizers" who failed to develop adequate agglutinin or antitoxin titers are recorded.

7. No relation was found between systemic reactions to inoculation and the development of high antibody or antitoxin titers.

We wish to acknowledge the assistance of Mrs. Ruth H. Silverman, R.N., in carrying out this study. We are greatly indebted to Mr. R. B. Clark, Supervisor of Clinical Research, Cutter Laboratories, Berkeley, Calif., for his ready cooperation and friendly assistance.

REFERENCES

1. Ramon, G.: Mixed Vaccinations, Internat. Clin. **1**: 241, 1939.
2. Lapin, J. H.: Combined Immunization of Infants Against Diphtheria, Tetanus and Whooping Cough, Am. J. Dis. Child. **63**: 225, 1942.
3. Lapin, J. H.: Mixed Immunization in Infancy and Childhood, J. PEDIAT. **22**: 439, 1943.
4. Daughtry-Denmark, L.: Whooping Cough Vaccine, Am. J. Dis. Child. **63**: 453, 1942.
5. Miller, J. J., Humber, J. B., and Dowrie, J. O.: Immunization with Combined Diphtheria and Tetanus Toxoids (Aluminum Hydroxide Adsorbed) Containing *Hemophilus pertussis* Vaccine, J. PEDIAT. **24**: 281, 1944.

6. Miller, J. J., and Silverberg, R. J.: Agglutinative Reaction in Relation to Pertussis and to Prophylactic Vaccination Against Pertussis with Description of a New Technic, J. Immunol. **37**: 207, 1939.
7. Flosdorf, E. W., McGuinness, A. C., Kimball, A. C., and Armstrong, J. G.: Studies with *H. Pertussis;* preparation and assay of hyperimmune human serum, J. PEDIAT. **19**: 638, 1941.
8. Miller, J. J., Jr., Silverberg, R. J., Saito T. M., and Humber, J. B.: An Agglutinative Reaction for Hemophilus pertussis; II. Its Relation to Clinical Immunity, J. PEDIAT. **22**: 644, 1943.
9. Sako, W.: Studies on Pertussis Immunization, J. PEDIAT. **30**: 29, 1947.
10. Ratner, B.: Allergy, Anaphylaxis and Immunotherapy, Baltimore, 1943, Williams and Wilkins Company, pp. 168-188.
11. Edsall, G.: Active Immunization, New Eng. J. Med. **235**: 256, 1946.
12. Sauer, L. W., Tucher, W. H., and Markley, E.: Immunity Responses to Mixtures of Diphtheria Toxoid and Pertussis Vaccine, J. A. M. A. **125**: 949, 1944.
13. Sako, W., Treuting W. L., Witt, D. B., and Nichamin, S. J.: Early Immunization Against Pertussis with Alum Precipitated Vaccine, J. A. M. A. **127**: 379, 1945.
14. Waddell, W. W., Jr., and L'Engle, C. S., Jr.: Immune Response to Early Administration of Pertussis Vaccine, J. PEDIAT. **29**: 487, 1946.
15. Miller, J. J., Jr., and Saito, T. M.: Concurrent Immunization Against Tetanus, Diphtheria, and Pertussis; Comparison of Fluid and Alum-precipitated Toxoids, J. PEDIAT. **21**: 31, 1942.
16. DeGara, P. F., and Mayer, S. A.: The Agglutinative Reaction for Hemophilus pertussis Following Whooping Cough and Following Immunization, J. PEDIAT. **30**: 171, 1947.
17. Adams, J. M., and Kimball, A. C.: To be published in J. PEDIAT.
18. di Sant'Agnese, P. A.: To be published.

MYOCARDIAL INFARCTION IN THE NEWBORN INFANT

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AN INTENSIVE search of the literature has failed to disclose any descriptions of myocardial infarction in the newborn infant, and only four instances in infancy. Ramsay and Crumrine[1] described the case of a 4-month-old female infant with thrombosis of the descending branch of the left coronary artery and resultant myocardial infarction. Ellis[2] reported a case in which there were several old infarcts associated with an aneurysm of the left ventricle in a 9-month-old hydrocephalic infant. Hughes and Perry[3] reported coronary thrombosis in an infant 7 weeks of age, and, most recently, Scott and Miller[4] described it in an 11-month-old infant. Our patients were aged 2 days and 10½ hours, respectively, and represent myocardial infarction in the newborn infant.

CASE HISTORIES

CASE 1.—A male Negro infant was delivered Sept. 25, 1945, spontaneously at term of a 28-year-old uniparous mother, at the Jewish Hospital of Brooklyn. The course of pregnancy had been entirely uneventful. The first stage of labor lasted 10½ hours and the second stage 25 minutes. Slight difficulty was encountered in delivering the shoulders and the vernix was stained yellow. At birth the child weighed 8 pounds, 2 ounces, its condition was good, and physical examination immediately after birth revealed no abnormalities. On the second day of life the child vomited green material on two occasions but thereafter took two feedings without any apparent difficulty. Two hours after the last feeding, and sixty-six hours after birth, the infant expired suddenly and unexpectedly.

The hemoglobin shortly after birth was 94 per cent with 2 erythroblasts per 100 white blood cells. The Rh factor of both mother and child was positive. The mother's blood Wasserman during pregnancy and after delivery was negative, although two years previously she had received a course of injections for syphilis.

Post-mortem Examination.—Post-mortem examination performed five hours after death revealed the following: There was no unusual amount of fluid in any of the serous cavities. The heart was markedly enlarged and weighed 47 Gm. (normal, 17 Gm.). The enlargement was principally right-sided and the right auricle and ventricle were dilated. The right and left ventricular walls were of equal thickness, both measuring 0.7 cm. The valves were delicate and the foramen ovale and ductus arteriosus were patent. The coronary ostia were patent, and the coronary vessels followed a normal course and were patent as far as they could be traced. The myocardium was red-brown except for an irregular area of bluish discoloration of the interventricular septum measuring 0.8 cm. in greatest diameter.

The lungs were buoyant and there were widespread areas of atelectasis.

The liver was congested and weighted 158 Gm. (normal, 78 Gm.).

The pancreas weighed 15 Gm. (normal, 2 Gm.) and was unusually firm.

The spleen was soft, congested, and the Malpighian corpuscles were prominent.

The mesenteric lymph nodes were enlarged.

The gastrointestinal tract, genitourinary tract, adrenals, and brain showed nothing remarkable.

From the Department of Laboratories, Division of Pathology, The Jewish Hospital of Brooklyn.

Microscopic Examination.—

Heart.—In a preparation of the interventricular septum of the heart, there is a large area of infarction involving the entire thickness of the wall with necrosis of the cardiac muscle fibers, hemorrhage, edema, and infiltration of the affected area with polymorphonuclear leucocytes. Within and about the infarcted area several branches of the coronary artery show pronounced thickening and fragmentation of the media with resultant narrowing of the lumina. The intima is uninvolved. In an elastic Van Giesen stained preparation, the internal elastic membrane is intact. The medial thickening is due to replacement of the smooth muscle by fibrous tissue. The external elastic membrane is fragmented and the media and adventitia are infiltrated with polymorphonuclear leucocytes, lymphocytes, and plasma cells. The lumina of many of the arteries and veins are occluded by pink-staining thrombotic material.

In sections taken from other areas of the heart many of the myocardial fibers are vacuolated, but Scharlach R and Best's carmine stains fail to reveal either fat or glycogen. The vessels in these regions show medial changes similar to, but less extensive than those in the region of the infarct. Collections of plasma cells surround some of these blood vessels. A few small arterioles are thrombosed and are surrounded by necrotic myocardial fibers. The epicardium is infiltrated with collections of plasma cells and lymphocytes.

Lungs.—Widespread areas of atelectasis with congestion of the vessels are present within the lungs. Many of the alveoli and smaller bronchioles contain large amounts of debris and blood pigment while others are filled with aspirated material. The small arteries and arterioles of the lung show fibrous thickening and fragmentation of the media. The lumina here are not narrowed. The media and adventitia are infiltrated with a few lymphocytes and plasma cells. Large collections of these cells as well as a few polymorphonuclears leucocytes are seen in many of the septal regions throughout both lungs.

Liver.—The liver sinusoids are markedly congested and the liver cell cords compressed. The liver cells are vacuolated and contain golden brown pigment granules. The Kupffer cells are prominent. Hematopoietic foci are extremely numerous.

Pancreas.—In preparations from the pancreas the lobular pattern is accentuated. The cytoarchitecture of the acini is distorted by an extensive fibrotic process which has replaced a large proportion of the parenchyma. The fibrous tissue is densely infiltrated with numerous round cells. The remaining acinar and duct structures appear relatively normal. Islands of Langerhans are present in usual numbers but appear somewhat loosely constructed. The blood vessels are not unusual.

Adrenals.—The adrenal glands show several small cortical adenomata but are otherwise not remarkable.

Kidneys.—In preparations from the kidneys, the cortex and medulla are well demarcated. The glomerular capillaries are congested. The epithelial cells lining the convoluted tubules contain golden brown pigment granules. Many of the collecting tubules contain casts of pink-staining debris, occasional red blood cells and their epithelial lining cells are poorly preserved. The blood vessels of the kidneys are somewhat distended, but are otherwise not remarkable.

Spleen.—The sinusoids of the spleen are congested. The Malpighian corpuscles are large but no germinal centers are seen. Foci of hematopoiesis are scattered throughout the splenic pulp. The blood vessels of the spleen are not remarkable.

Bone.—The metaphysis of a rib taken for section is thin and straight. The periosteum is intact and the trabeculae are not remarkable.

Bone Marrow.—The bone marrow shows moderate hyperplasia of the erythrogenic and myeloid elements.

Anatomic Diagnosis.—Sclerosis, medial, of coronary arteries; thrombi in coronary arteries; myomalacia cordis; hypertrophy and dilatation of heart; pancreatitis, chronic; extramedullary hematopoiesis in liver and spleen; atelectasis and hemorrhage in lungs; congestion of viscera.

CASE 2.—This white male infant was born at term on Jan. 12, 1946, at the Jewish Hospital of Brooklyn. The mother was a 42-year-old gravida V, para ii. The first child died within twenty-four hours of birth of unknown cause. The second and fourth pregnancies were terminated by early miscarriages. The third child is living, although at 6 months of age, a retinal glioma of the left eye was found, and the eye was enucleated. The mother and father are both Rh positive and the maternal blood Wassermann is negative.

The present pregnancy was uneventful. The mother was admitted with ruptured membranes and mild irregular pains. Rectal examination revealed a double footling breech presentation. On the day following admission pituitrin was administered in six divided doses of one minim each, given at twenty-minute intervals in an effort to stimulate labor. This was partly successful, and produced mild uterine contractions which occurred every five minutes. Two hours later three additional 1 minim dose of pituitrin were given at twenty-minute intervals. Two minutes before delivery, the fetal heart, which until that time had been regular at a rate of 140 beats per minute, could not be heard. An assisted breech delivery was performed a few minutes after the final dose of pituitrin. A Mariceau-Smellie-Viet maneuver was performed to deliver the aftercoming head. The first and second stages of labor lasted a total of four hours, twenty minutes.

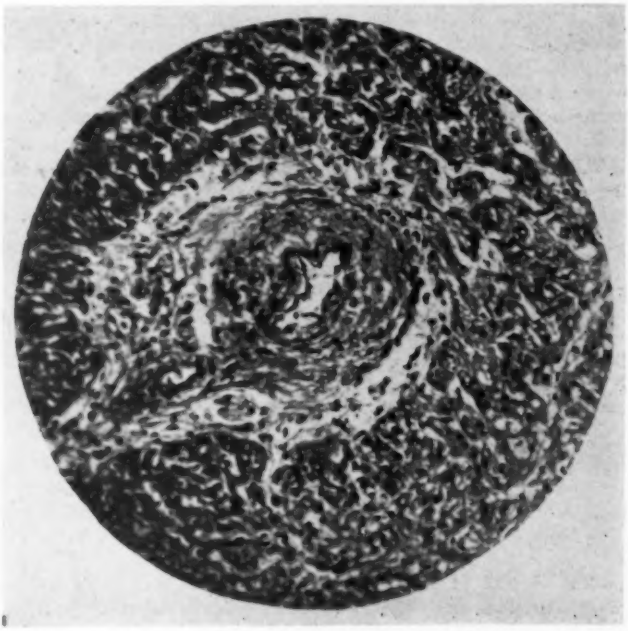

Fig. 1.—(Case 1.) Section of left ventricle showing artery with thickened media and perivascular infiltration of round cells. H and E ×112.

The condition of the child at birth was very poor. The infant was cyanotic, the respirations were absent or depressed, but the heart action was regular. The child weighed 4 pounds, 8 ounces. Oxygen was administered for one hour. A thin, foamy material had to be aspirated from the trachea. The respirations remained inadequate, there was intercostal retraction, and the lungs were atelectatic. Ten and one half hours after birth the infant expired.

Post-mortem Examination.—Post-mortem examination performed four hours after death revealed gross significant findings only in the thoracic organs. The heart weighed 18 Gm. The posterior wall of the left ventricle was hemorrhagic over an area measuring 2.3 × 1.5 cm. The center of this area was yellow in color and the myocardium was softer than elsewhere. The hemorrhagic infarct involved the entire thickness of the wall as well as the posterior papillary muscle of the mitral valve. The heart was not dilated and the right ventricle measured 0.3 cm. and the left 0.5 cm. in thickness. The coronary ostia were patent. The coronary vessels followed the usual course and were patent as far as they could be traced. A vein in the region of the infarct contained a large thrombus. The lungs were congested and atelectatic. There was a small amount of hemorrhagic fluid in the subarachnoid space. The other organs showed nothing of note.

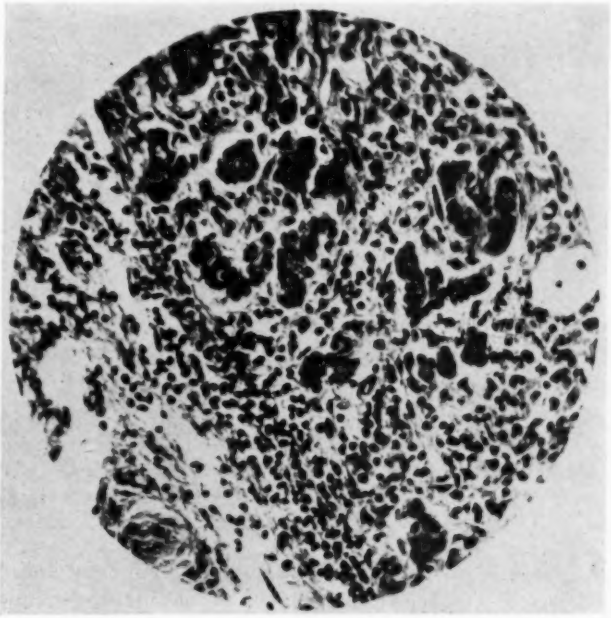

Fig. 2.—(Case 1.) Section of pancreas showing marked fibrosis and cellular infiltration. H and E ×200.

Microscopic Examination.—

Heart.—In sections of the posterior wall of the left ventricle almost the entire thickness is necrotic. The myocardium is hemorrhagic and individual muscle fibers either cannot be seen or are ghostlike in character. Replacing the usual structures is an homogeneous pink-staining material, fibrin, and large pools of blood. Scattered throughout are numerous poorly preserved nuclei, many of which are pyknotic or karyorrhectic. Many blood vessels can be identified whose lumina are completely occluded by thrombotic material and whose walls merge with the surrounding necrotic tissue. At the periphery of the infarcted area numerous distended capillaries are seen. In addition there are collections of polymorphonuclear leucocytes as well as occasional round cells. These collections of cells are especially prominent beneath the endocardium. A few spindle-shaped fibroblastic cells are also seen extending into the infarct. Elsewhere the myocardium is fairly well preserved. The fibers are slender and nuclei stain well. Cross striations are indistinct. The sarcoplasm contains occasional small vacuoles. The interstitial connective tissue is delicate and harbors distended blood vessels whose

walls are not thickened. A few small petechial hemorrhages are also seen in places distant from the infarct.

Lungs.—Very few of the alveoli are aerated and the bronchioles are collapsed. Many alveoli are filled with an amorphous pink-staining material, red blood cells, and brown pigment granules. Large macrophages containing pigment are also seen. The vessels are distended but are otherwise not remarkable.

Anatomic Diagnosis.—Thrombi in coronary arteries and veins; myomalacia cordis; congestion of viscera.

Fig. 3.—(Case 2.) View of posterior surface of heart and lungs showing the large area of hemorrhagic infarction with central necrosis.

DISCUSSION

In recent years it has become increasingly apparent that coronary artery disease with myocardial damage is not confined to the older age groups. In 1927, White and Mudd[5] discussed 418 cases of coronary thrombosis, 3 per cent of which occurred in patients under the age of 40. In 1942, Reitman, Greenwood and Kler[6] summarized the literature and described 221 cases of coronary thrombosis in individuals less than 40 years of age. Thirty-four of these occurred in patients under the age of 30. French and Dock[7] in 1944 reviewed 100 autopsies performed during World War II on American soldiers 20 to 36 years of age in whom coronary sclerosis was found to be the cause of death. Zacks[8] collected 8 cases, and added one of his own, of coronary thrombosis with myocardial infarction occurring during the second decade of life.

As has previously been noted, coronary thrombosis in the very young is extremely uncommon and only four instances were found in the literature. The usual causes of coronary artery disease are very rare in infancy, although Guild and associates[9] have collected twenty-two cases of coronary artery disease in childhood. Furthermore, despite the occurrence of congenital coronary artery

anomalies, secondary thrombosis and myomalacia are highly unusual, even in those patients who survive the periods of infancy and childhood. A recent example is that of Knop and Bennet[10] who described sudden death in a 5-day-old female infant who had a single coronary artery with a hypoplastic left branch. Frank myomalacia cordis was not present, although vacuolar degeneration of the myocardium was noted.

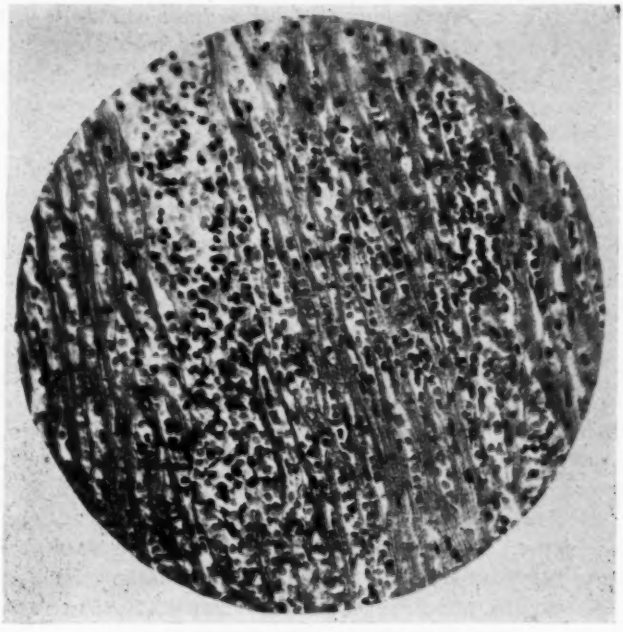

Fig. 4.—(Case 2.) Section from ventricle with hemorrhage, destruction of myocardial cells, and cellular infiltration. H and E ×200.

Brown and Richter[11] found six published cases of "medial coronary sclerosis" occurring in infancy, to which they added one of their own. These cases showed calcification of the internal elastic membrane of all the arteries of the body, accompanied by intimal proliferation resulting at times in coronary occlusion and myocardial ischemia with areas suggestive of infarction. These foci of necrosis could not be distinguished from areas of myocardial necrosis such as those seen in rats poisoned by irradiated ergosterol. Some alteration in the calcium-phosphorous metabolism of the body was postulated in these cases. A similar condition has been produced in experimental animals by administering large doses of parathormone[12] or Vitamin D.[13]

The two cases presented here are unique. So far as is known they are the first descriptions of myocardial infarction in the newborn infant. Thus they complete the picture and indicate that myomalacia cordis may occur at any age of life.

The first case presented might have been overlooked, because although sections were taken through the area of discoloration in the septum the possibility of an infarct was not considered until the histologic sections were seen. The most probable pathogenesis in this case was intrauterine infection of fairly long standing which affected the small arteries of the heart and lung and also resulted in a fibrosing pancreatitis. It must be noted, however, that there was no history of any serious illness in the mother during pregnancy. The Wassermann test for syphilis was negative on two occasions and although the pancreatic lesions superficially resembled those of syphilis, no other manifestations of congenital syphilis were present in the skin, lungs, liver, spleen, or bones. Without characteristic involvement of any of these organs, a diagnosis of syphilis was felt to be untenable. Furthermore, special stains of the viscera failed to reveal spirochetes. The enlargement of the heart in this case was quite pronounced and can probably be explained on the basis of ischemia due to the narrowing of the lumina of the smaller arteries and arterioles. Support is lent to this view by Davis and Blumgart[15] and others who believe that cardiac hypertrophy is not necessarily due to an increased load upon the heart but may be the result of "impaired nutrition of the muscle fibers which causes them to undergo stretching and consequent hypertrophy."

There was no doubt on gross examination of our second case that we were dealing with a very recent hemorrhagic infarct of the heart. None of the other tissues contained hemorrhagic areas so that there was nothing to indicate that this was a local manifestation of hemorrhagic disease of the newborn. Furthermore, no cases of this disease have been reported in which the myocardium was involved. The Rh studies were noncontributory. The pathogenic process in this case is quite obscure. Several possible explanations must be considered, however. The pressor and oxytocic fractions of the posterior pituitary gland extracts used in obstetrical practice cannot be completely separated from one another. The pressor substance of the gland causes vasoconstriction of the coronary vessels.[14] Undoubtedly this substance administered to the mother also enters the fetal circulation. Excessive retardation of blood flow in the conorary circulation may have been produced, resulting in thrombosis of the blood vessels. Another possibility is that the forceful uterine contractions brought about by the administration of pituitrin may have produced too great a pressure on the after-coming head. This may have caused an increase in the intracranial pressure leading to vasoconstriction. A small amount of blood-tinged fluid was present in the cranial cavity. Direct trauma to the precordium during labor or delivery cannot be excluded.

SUMMARY

Two cases of myocardial infarction occurring in the neonatal period are presented. This condition has not been previously described in newborn infants. It is possible that such a lesion may be present and yet be unnoticed at autopsy examination.

REFERENCES

1. Ramsey, R. E., and Crumrine, R. M.: Coronary Thrombosis in an Infant Aged Four Months, Am. J. Dis. Child. **42**: 107, 1931.
2. Ellis, R. W. B.: Infarcts and Aneurysm of Heart in an Infant of Nine Months, Proc. Roy. Soc. Med. **28**: 1333, 1935.
3. Hughes, F. W. T., and Perry, C. B.: Senile Arterial Changes in a Child Aged Seven Weeks, Bristol Med. Chir. J. **46**: 219, 1929.
4. Scott, E. P., and Miller, A. J.: Coronary Thrombosis. Report of a Case in an Infant Eleven Months of Age, J. PEDIAT. **28**: 478, 1946.
5. White, P. D., and Mudd, S. G.: Angina Pectoris in Young People, Am. Heart J. 3: 1, 1927.
6. Reitman, N., Greenwood, W. R., and Kler, J. H.: Coronary Thrombosis in a Young Diabetic, Am. J. M. Sc. **203**: 792, 1942.
7. French, A. J., and Dock, W.: Fatal Coronary Arteriosclerosis in Young Soldiers, J. A. M. A. **124**: 1233, 1944.
8. Zacks, L.: Coronary Thrombosis and Myocardial Infarction in Youth, Am. Heart J. **26**: 269, 1943.
9. Guild, H. G., Kindale, F. B., and Gibson, T. A.: Arteriosclerosis in Childhood, Johns Hopkins Hosp. **62**: 159, 1938.
10. Knop, C. Q., and Bennet, W. A.: Sudden Death from Coronary Insufficiency: Report of Case of an Infant. Proc. Staff Meet., Mayo Clinic **19**: 574, 1944.
11. Brown, C. E., and Richter, I. M.: Medial Coronary Sclerosis in Infancy Arch. Path. **31**: 449, 1941.
12. Hueper, W. C.: Metastatic Calcification in the Organs of the Dog After Injections of Parathyroid Extract. Arch. Path. 3: 14, 1927.
13. Shohl, A. T., Goldblatt, H., and Brown, H. B.: The Pathological Effects on Rats of Excess Irradiated Ergosterol, J. Clin. Investigation **8**: 505, 1931.
14. Goodman, L., and Gillman, A.: The Pharmacological Basis of Therapeutics. N. Y., 1941, The Macmillan Company.
15. Davis, D., and Blumgart, H. L.: Cardiac Hypertrophy: Its Relation to Coronary Arteriosclerosis and Congestive Heart Failure, Ann. Int. Med. **11**: 1024, 1937.

TREATMENT OF DIABETIC ACIDOSIS

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RECOGNITION and treatment of serious disturbances of acid-base balance in infants and children continue to constitute an important part of hospital pediatric practice. During the 24-year period (1923 to 1946) in which one of us (A. F. H.) was particularly interested in the problem as it presented itself at the St. Louis Children's Hospital, there were encountered 1,465 instances of *metabolic acidosis* which were diagnosed by chemical determination of blood $BHCO_3$. Unquestionably, many cases were missed, particularly those of mild degree in moribund children. Relative to the total number of admissions, the incidence of metabolic acidosis is approximately 2 per cent. The potential seriousness of the condition and the technical aspects of therapy, however, lend much more importance to it.

A rough breakdown of these children is shown in Table I. It will be seen immediately that severe gastrointestinal disturbance referred to as *diarrhea* accounts for approximately three-sevenths or 44.7 per cent of the total number and that *diabetes mellitus, renal disease, severe infection,* and *other causes* each account for approximately one-seventh.

TABLE I. INCIDENCE OF METABOLIC ACIDOSIS, 1923-1946 INCLUSIVE

	1923-33	1934-46	TOTAL	PER CENT
1. Diarrhea	178	477	655	44.7
2. Diabetes mellitus	78	131	209	14.2
3. Renal disease	78	130	208	14.2
4. Infection or moribund state	44	142	186	12.6
5. Other causes	71	136	207	14.2
		Total cases	1,465	99.9

During the first few years of the study, therapy excluded any *alkali administration per se* except for a few cases of diabetic acidosis,[1] and relied chiefly on administration of *dextrose* and *NaCl* and the antiketogenic effects of *insulin*. During this era, the most prominent champions of this method of therapy which excluded alkali administration were Gamble[2] and his co-workers in Boston and Hoag[3, 4] and his co-workers in New York in the field of *pediatrics,* and Joslin[5, 6] and his school and Peters[7] and his co-workers in Boston in the field of *internal medicine.*

Due chiefly to the influence of Marriott, one of us (A. F. H.) undertook a restudy of the possibilities of *direct* alkali administration and soon became enthusiastic about the results obtained by the early administration of $NaHCO_3$ along with all other indicated treatment.[8, 9] Shortly afterward, Na-lactate was substituted for $NaHCO_3$[10-14] because lactate possessed several important advantages over bicarbonate. There was also substituted a *hypotonic Ringer's*

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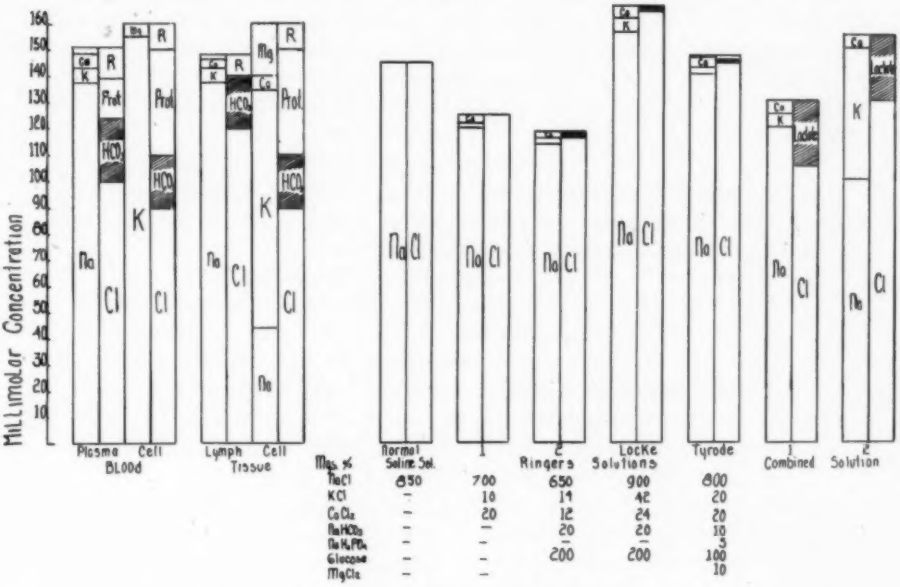
solution for isotonic NaCl for two reasons: (1) to secure additional water administration with reference to salt and in that way to help overcome dehydration and promote diuresis, (2) to supply K, Ca, and Mg, as well as Na. Our initial concept was to offer the body an excess of water, Na, K, Ca, Mg, Cl, and even potential HCO_3 in the form of excess of fixed base over fixed acid, so that by selective reabsorption the renal tubules could retain what was desirable and reject what was not, in the reconstitution of extracellular fluid.



Composition of Normal Body Fluids and Physiological Saline Solutions

Fig. 1.

Shortly after developing lactate-Ringer's solution for repair of extracellular fluid, one of us (A. F. H.) became concerned with *intracellular* fluid composition and attempted to make up for K deficiency by administering combined solution No. 2 (Fig. 1) parenterally after combined solution No. 1 (lactate-Ringer's solution) had been given for a while. After reporting on these studies to the American Pediatric Society at its St. Louis meeting in 1929, this attempt was abandoned both because no special improvement was noted and because sometimes the richer potassium solution seemed toxic. In its place were gradually substituted more vigorous attempts to aid the cells by more *complete parenteral feeding* in the form of whole blood, plasma, "enriched" plasma to provide essential fatty acids, vitamins, as well as glucose and minerals.[15-17] During this period of study, which takes us up to the present time, other workers, including Butler,[18] Levine,[19] and Dodd[20] were pursuing almost identical objectives.

During the past year, however, Darrow has most definitely demonstrated K loss, particularly as a result of diarrhea, and reopened the advisability of early direct replacement of potassium.[21] It seems, therefore, very desirable to us at this time to analyze carefully results which have been obtained without a K-fortified solution, so that later when sufficient experience with special potassium therapy has been obtained, comparison of the two methods will be possible.

In this analysis we wish particularly to stress ketone-body acidosis and especially that of diabetes mellitus, reserving for later consideration that type of acidosis based on diarrhea or renal failure in which alkali therapy is even more imperative. We shall stress pathways of recovery as related particularly to *dosage* of *administered alkali* and *time* required for complete or almost complete recovery.

DOSAGE OF ALKALI

Let us first look into the matter of dosage of alkali as recommended by various pediatric authorities for the correction of acidosis in general where attempts have been made to apply formulae.

Hartmann-Senn.—(J. Clin. Investigation, p. 334, March, 1932.)

"60 – CO_2 cont. × .3 body weight (Kg.) = c.c. molar Na-lactate or $NaHCO_3$"

or

$BHCO_3$ deficit in mM/L. × .67 body weight (Kg.) = c.c. molar Na-lactate

Example for severe acidosis of 20 mM $BHCO_3$ deficit (24 – 4) × .67 = 13.4 mM Na-lactate *per Kg.*

Later, however, Hartmann, Perley and associates (J. PEDIAT. **13**: Nov., 1938), and Hartmann and associates, in many subsequent statements, advised administering first 60 c.c. ⅙ molar per kilogram and later an additional dose of 30 c.c. ⅙ molar per kilogram or more if it seemed advisable. This, of course, would amount to an initial dose of 10 mM per kilogram with a second of 5 or more.

Mitchell-Nelson.—Textbook of Pediatrics, ed. 4, p. 169, 1945.

Apparently assume an equally sharing body water content of 0.7 body weight, and state

"CO_2 deficit in m.eq./L. × body weight in kilogram × 0.059 = Gm. $NaHCO_3$."

This formula could be rewritten as follows:

$BHCO_3$ deficit mM/L. × 0.7 body weight (Kg.) = mM $NaHCO_3$ or Na-lactate. Example (24 – 4) × 0.7 = 14 c.c. mM Na-lactate per kilogram.

On the same page, however, a statement directly referring to Na-lactate appears which is incompatible with the above formula and is as follows:

"1 c.c. of ⅙ molar sodium lactate solution per kilogram body weight will increase the plasma bicarbonate 0.8 m.eq. per liter, or 1.8 volumes per cent of CO_2 per 100 c.c. of plasma."

With the use of the Mitchell-Nelson formula, only 30 per cent of such increase should be expected, since:

1 c.c. ⅙ molar Na-lactate per kilogram = .167 m.eq. HCO_3 per kilogram = $\frac{.167}{.7}$ m.eq./L. body water = .24 m.eq./L. = .54 vol. per cent CO_2 = 30 per cent of the stated rise.

Holt and McIntosh.—Holt's Diseases of Infancy and Childhood, ed. 11, p. 228.

"Wt. (lb.) × 55 – CO_2 (combining power) = cubic centimeters ⅙ M. Na-lactate of $NaHCO_3$."

Example, 2.2 × 44.8 = 98.8 c.c. ⅙ molar or approximately 15 mM per kilogram.

Darrow.—New England J. Med. (July), 1945.

"0.5 body wt. × $BHCO_3$ deficit in mM/L. = mM $NaHCO_3$ or Na-lactate."

Example, 0.5 × (24 – 4) = mM per kilogram.

or

60 c.c. ⅙ molar $NaHCO_3$ or Na-lactate per kilogram.

A summary of the above recommended dosages of alkali is given in Table II. While all these formulae are in essential agreement, they are all more or less empirically derived or assume distribution of injected or converted alkali throughout the body fluids without dissipation or enhancement. But let us look into this matter more closely, for it is somewhat more complicated.

TABLE II. CALCULATION OF ALKALI DOSAGE

AUTHOR	FORMULA	mM PER KG. BODY WT.
Darrow New Eng. J. Med., July, 1945	0.5 body wt. (Kg.) × $BHCO_3$ deficit mM/L. = mM $NaHCO_3$ or Na-lactate	10.0
Hartmann-Senn J. Clin. Invest., p. 334, Mar., 1932	60 – CO_2 cont. × .3 body wt. (Kg.) = c.c. molar Na-lactate or $NaHCO_3$	13.4
Mitchell-Nelson Textbook Pediatrics, 4th ed., p. 169, 1945	CO_2 deficit M.Eq./L. × body wt. (Kg.) × .059 = Gm. $NaHCO_3$	14.0
Holt and McIntosh Holt's Diseases of Infancy and Childhood, 11th ed., p. 228	Wt. (lb.) × (55 – CO_2 combining power) = c.c. ⅙ M. Na-lactate or $NaHCO_3$	15.0
Hartmann-Perley et al. J. PEDIAT., 13, Nov., 1938	60 c.c. ⅙ M. for initial dose 30 c.c. ⅙ M. or more later if needed	10-15 or > 15

Let us first enumerate factors which either always operate or sometimes operate during recovery from severe acidemia and which would prevent administered Na-lactate or $NaHCO_3$ from appearing quantitatively as $BHCO_3$ in body fluids in a reasonably short time (six to twelve hours).

1. All blood buffers other than H_2CO_3, but particularly hemoglobin, would claim more base with rising pH. For a pH shift of 7.4 to 7.0, while $BHCO_3$ undergoes a reduction of 18 mM per liter, other blood buffers yield 10 m.eq. per liter of alkali.[22] For a shift in the reverse direction, 28 mM of $BHCO_3$

per liter of blood would have to be added to secure an increase of 18 mM. Therefore, to secure an increase of 20 mM $BHCO_3$ per liter of blood, a total of 31 mM would have to be given, or an additional 55 per cent.

2. If, during the period of recovery from acidemia, hemoglobin becomes more fully oxygenated, which seems usually to occur, still more base would be claimed than the pH shift alone would necessitate.

3. Fixed tissue buffers would be expected to behave in a similar fashion.

4. If recovery is attended by permanent gain in body fluid content, which usually occurs to the extent of 5 to 10 per cent of the original body weight, or 7.5 to 15 per cent of the original body fluid, there would be a corresponding decrease of $BHCO_3$ concentration.

5. There may exist a continued trend toward development of acidosis, such as continued loss of alkali as the result of continued severe diarrhea, continued excessive secretion of alkaline urine, or continued abnormal acid formation, such as in the ketosis of salicylate intoxication, milkweed poisoning, or in diabetes mellitus when insulin effect is inadequate. In this category also might be included occasionally increased lactic acid formation as a result of convulsions, unusual activity, and tissue anoxia.

6. Some loss of Na-lactate by excretion into the urine may occur. When diuresis is not immediate, and, therefore, in almost all cases of dehydration except those due purely to primary polyuria, such loss might be expected to be less than 10 per cent.

7. There might possibly exist interference with the utilization of lactate such as might result from continued tissue anoxia or severe liver damage. Such interference would be expected to lead to persistent high blood concentrations of lactate and possibly more than usual excretion into the urine. Extensive observation over many years has proved that such interference does not occur except in subjects actually dying. Delay of a few hours in the complete utilization of Na-lactate is, however, occasionally noted in apparently moribund subjects who eventually recover.

Let us now enumerate factors which would tend to supplement and enhance the effect of conversion of Na-lactate into $NaHCO_3$ in the tissue fluids, or increase the effect of administered $NaHCO_3$.

1. Pre-existing lactate accumulation, which disappears simultaneously with the metabolism of injected lactate, as a result of improvement of circulation, recovery from tissue anoxia, or reduction in lactic acid formation. Such a factor as this is especially significant in subjects in a postconvulsive state, or in subjects in whom extreme anhydremia has been relieved during the time period under consideration.

2. Simultaneous abolition of ketosis, such as occurs in the diabetic receiving insulin, in properly treated salicylate intoxication, milkweed poisoning, starvation, and certain infections. The significance of this factor depends both on the original extent of ketone acid accumulation and on their rate of oxidative removal in the tissues.

3. Renal activity which results in quantitatively significant tubular reabsorption of fixed base and rejection of fixed or organic acid from glomerular filtrate.

4. Extraneous alkali administration, such as frequently overlooked but often significant ingestion of fruit juices.

From even such a brief consideration as the above, it would seem improbable that any formula for calculation of an optimal dose of alkali for the relief of acidosis would work equally well for all cases. This would especially be true if variable pH change in particular were not included in the formula.

What would seem both possible and highly desirable would be the calculation of an initial dose of alkali which would be sufficient at least to relieve all dangerous degrees of acidosis, and yet preclude all risk of development of dangerous degrees of alkalosis, and at the same time accomplish such an end in just a few hours. Final complete correction could then be accomplished at a slower rate without risk of unnecessary continuation of the terrible load which the subject with a severe degree of acidosis is forced to bear.

We feel that the methods developed in the St. Louis Children's Hospital for the past fifteen years meet the above requirements and have proved highly satisfactory for correction of both acidosis and alkalosis, and we now wish to submit further evidence for such a claim. Rather than cover the whole subject of acid-base balance, we prefer to omit the types of acidosis (e.g., renal—diarrheal) in which there is more general agreement as to the need for alkali replacement, and instead shall concentrate on diabetic acidosis.

Let us first analyze findings characteristic of severe diabetic acidosis.

By definition, there is always extensive $BHCO_3$ deficit in the body fluids. For purposes of analysis we have classified severity of acidosis as follows (Table III): All subjects with severe diabetic acidosis should exhibit some degree of air hunger or hyperpnea, which would be an expression of respiratory defense in compensation for $BHCO_3$ reduction. The degree of hyperpnea is variable, however, and seems not very closely related to the $BHCO_3$ content. Indeed, often with the general improvement which follows shortly after beginning of treatment, hyperpnea becomes more evident for a while, rather than less. This point is especially evident in moving pictures which we have made perpnea one would, therefore, expect variation in initial pH of the plasma, and, indeed, such is the case. In subsequent discussion we have made use both of the Steinhaus-Hastings[23] and of the Gamble[24] type of chart to illus- at intervals during treatment. With variable degrees of compensatory hy- trate this point.

From these instructive data which will be discussed later it can be noted that in some individuals there is no adjustment whatsoever of H_2CO_3 to change in $BHCO_3$. (Parenthetically it may be stated that it is such individuals as

TABLE III. CLASSIFICATION OF SEVERITY OF ACIDOSIS

Extreme acidosis (CO_2 cont. 6-14.9 vol. %) ($BHCO_3$ 2.5-6.3 mM/L.)	Moderate acidosis (CO_2 cont. 25-34.9 vol. %) ($BHCO_3$ 10.7-14.8 mM/L.)
Severe acidosis (CO_2 cont. 15-24.9 vol. %) ($BHCO_3$ 6.4-10.6 mM/L.)	Mild acidosis (CO_2 cont. 35-44.9 vol. %) ($BHCO_3$ 14.9-19.1 mM/L.)

TABLE IV. RECOVERY FROM DIABETIC ACIDOSIS

NO.	HISTORY NO.	DATE	AGE	pH	$BHCO_3$ mM/L.	CL M.EQ./L.	PROTEIN GM./100 C.C.	H_2O GM./100 C.C.	FREEZING POINT M.OSM./L.	GLUCOSE MG./100 C.C.	N.P.N. MG./100 C.C.	TOTAL BASE M.EQ./L.	TREATMENT INTERVAL (HR.)
1	A-599	2/11/25	12	6.97	4.7	98.8	--	--	--	475	30.8	--	12
		2/12/25		7.30	13.4	--	--	--	--	175	38.0	--	
2	A-365	6/ 3/26	10	7.17	6.2	92.0	9.99	--	--	516	52.2	128	22
		6/ 4/26		--	19.1	95.0	8.81	--	--	112	46.8	138	
3	C-1636	8/24/26	12	7.10	6.4	--	--	--	--	470	--	--	15
		8/24/26		7.38	21.5	--	--	--	--	226	--	--	
4	A-1394	9/16/26	8	7.00	4.7	84.8	9.99	--	351	488	37.8	119	20
		9/17/26		7.23	14.3	90.0	8.49	--	284	91	41.8	123	
5	B-1826	4/ 4/27	7	7.23	10.0	96.0	8.28	--	--	210	26.0	--	24
		4/ 5/27		--	20.6	98.0	8.28	--	--	86	--	--	
6	C-1650	5/26/28	15	7.10	10.0	92.8	8.23	91.1	346	492	36.6	150	23
		5/27/28		7.35	15.6	98.5	8.31	92.4	282	148	27.7	152	
7	A-1739	1/31/27	12	7.10	6.4	96.0	9.56	--	413	413	33.0	133	26
		2/ 1/27		--	14.5	--	7.20	--	--	76	--	--	
8	A-1394	4/ 3/28	9	7.00	8.0	89.1	7.88	88.6	394	707	48.0	141	21
		4/ 4/28		7.57	39.3	84.8	5.90	94.2	452	40	46.4	154	
9	A-1394	6/ 6/28	9	6.95	2.9	80.8	6.80	88.5	--	922	--	127	8
		6/ 7/28		7.43	22.8	90.0	7.18	92.5	--	22	--	143	

TABLE V. RECOVERY FROM DIABETIC ACIDOSIS

NO.	HISTORY NO.	DATE	AGE	pH	$BHCO_3$ mM/L.	CL M.EQ./L.	PROTEIN GM./100 C.C.	GLUCOSE MG./100 C.C.	N.P.N. MG./100 C.C.	TREATMENT INTERVAL (HR.)
10	I-429	2/29/32	9	7.00	5.8	91.8	7.60	543	33.0	20
		3/ 1/32		7.41	23.0	--	--	172	--	
11	L-1807	8/ 5/36	5	7.00	8.6	--	--	290	--	24
		8/ 6/36		--	29.7	--	--	80	--	
12	J-373	8/ 6/36	10	7.01	8.6	--	--	372	--	25
		8/ 7/36		--	23.2	--	--	77	18.0	
13	L-2531	9/ 5/37	8	--	3.8	--	--	344	--	17
		9/ 6/37		7.41	22.1	--	--	20	--	
14	L-1850	10/ 5/37	10	7.08	4.0	--	6.74	345	27.0	6
		10/ 5/37		7.38	17.1	--	--	64	--	
15	N-2070	11/11/37	12	7.30	12.4	--	7.41	355	27.0	12
		11/11/37		7.43	26.4	--	--	120	--	
16	O-151	1/ 9/38	12	6.95	3.1	94.0	7.46	459	41.0	21
		1/10/38		7.43	25.9	94.0	5.96	178	37.0	
17	K-372	6/27/39	14	6.91	2.8	--	--	448	--	28
		6/28/39		7.43	19.1	--	--	207	--	
18	K-372	12/ 2/39	14	7.04	5.0	--	--	345	--	11
		12/ 2/39		--	23.2	--	--	--	--	
19	P-1200	4/18/40	7	7.16	5.7	--	--	640	--	6
		4/18/40		7.53	26.6	--	--	235	--	
20	Q-1143	4/25/40	11	6.94	4.5	--	--	758	--	17
		4/26/40		--	29.2	--	--	59	--	
21	Q-1143	6/12/40	11	7.17	7.6	--	--	357	--	21
		6/13/40		--	--	--	--	106	--	
22	Q-1927	9/ 5/40	14	7.20	7.7	--	--	647	--	7
				--	23.8	--	--	--	--	
23	S-1520	3/23/45	13	6.95	4.4	103.0	8.11	405	30.5	24
		3/24/45		--	--	95.8	5.70	--	24.0	
24	T-1619	12/ 6/46	13	6.95	3.8	100.0	--	672	35.0	24
		12/ 7/46		7.47	28.7	--	--	158	--	

these who need treatment most promptly and who require the most alkali for complete correction.) *Average* respiratory adjustment to severe acidosis is well under 50 per cent complete.

All subjects with severe diabetic acidosis are dehydrated and permanent retention of fluid after recovery usually is at least 5 and may sometimes be 10 per cent of the initial body weight. In some, moreover, dehydration of the blood, or anhydremia or hemoconcentration as it is more frequently called, is so severe that the subject appears in shock and is in circulatory failure. All subjects have a chloride deficit as well as a bicarbonate deficit, apparently chiefly the result of vomiting, which almost always attends the development of acidosis. Due to the initial hemoconcentration, however, the extent of such chloride deficit is not revealed by the original plasma value. All have ketosis, but the degree to which ketosis accounts for $BHCO_3$ deficit is very variable. In many instances when ketosis has been completely relieved, there is still significant $BHCO_3$ and total fixed base deficit. It is our clinical impression that well-nourished children who develop acidosis quickly and whose acidosis has been of short duration show relatively the most intense ketosis and are best adjusted to $BHCO_3$ deficit, whereas the poorly-nourished child in acidosis longer will show relatively less ketosis, more fixed base deficit, and will have the lower pH_s values. The glycogen reserves are apparently low in all subjects and in all there are also both hyperglycemia and glycosuria. In the following lantern slides are data referable to some of these points which describe initial conditions found in the twenty-four children in whom plasma pH determinations were made (Tables IV and V), as well as conditions some time later.

With the above characteristics of severe diabetic acidosis in mind, we can now logically list the main objectives in treatment, and in the order of their

TABLE VI. OBJECTIVES AND THE MEANS BY WHICH THEY MAY BE ACCOMPLISHED IN THE TREATMENT OF SEVERE DIABETIC ACIDOSIS
(LISTED IN THE ORDER OF THEIR IMPORTANCE)

OBJECTIVES	MEANS
1. Restoration of body fluid pH and $BHCO_3$ (rapidly, completely, and safely)	By indirect effect of metabolism of Na $L^{(+)}$-lactate By indirect effect of metabolism of Na $D^{(-)}$-lactate By indirect effect of abolition of ketosis (insulin) By indirect effect of renal activity (Ringer's sol.)
2. Relief of anhydremia and dehydration (rapidly but safely)	By isotonic Na-lactate solution By hypotonic Ringer's solution By plasma protein
3. Restoration of normal total electrolyte pattern of body fluids	By Ringer's solution By Na-lactate solution By renal activity By abolition of ketosis, polyuria, vomiting
4. Abolition of ketosis	By insulin
5. Restoration of glycogen reserves	By insulin By effect of Na $L^{(+)}$-lactate
6. Reduction of hyperglycemia and glycosuria	By insulin
Average requirements	Insulin—2 units/Kg. body wt. ⅙ M. Na-lactate sol.—60-90 c.c. per Kg. body wt. Ringer's solution—40 ± c.c. per Kg. body wt.

importance (Table VI). A better understanding of our treatment might be had if we compare it to the types of treatment in current use. (Table VII).

In this comparison it should be noted that we retain the insulin and water components, substitute hypotonic Ringer's solution for isotonic NaCl, and isotonic Na-lactate for $NaHCO_3$, and secure from lactate sufficient glucogenic effect to render early administration of dextrose unnecessary (60 c.c. ⅙ M. Na-lactate per kilogram possesses a glucose potential of 0.9 Gm. per kilogram).

TABLE VII. TREATMENTS PROPOSED FOR DIABETIC ACIDOSIS

JOSLIN ET AL.	PETERS ET AL.	HARTMANN ET AL.
Insulin q.s. ad. for speedy abolition of ketosis	+	+
Isotonic NaCl for dehydration	+	Hypotonic Ringer's
Oral water, fruit juices for dehydration	Not relied upon	Not relied upon
----------	$NaHCO_3$	Na-lactate
----------	Dextrose I.V.	----(Sufficient glucogenic effect from Na-lactate)

ANALYSIS OF RESULTS OF TREATMENT

Let us first consider the behavior of plasma pH and $BHCO_3$, because together they define the acid-base balance of the blood. We have twenty-four subjects in whom initial acid-base balances were determined. (Figs. 2 and 3.)

As mentioned before, it will be seen at a glance that respiration never fully compensates for $BHCO_3$ deficit, but that instead, acid-base balances sometimes indicate no adjustment whatsoever of H_2CO_3 to change in $BHCO_3$. It should also be noted that when $BHCO_3$ is reduced to the value of 4 to 5 mM per liter, the pH is rarely ever above 7.0.

A reasonable explanation for such relative respiratory failure is that the child is simply too weak to maintain normally maximal respiratory effort and normal pulmonary circulation. As will be noted in the movies, the first evidence of improvement after treatment begins is increase in both rate and depth of respiration, together with obvious general increase in strength.

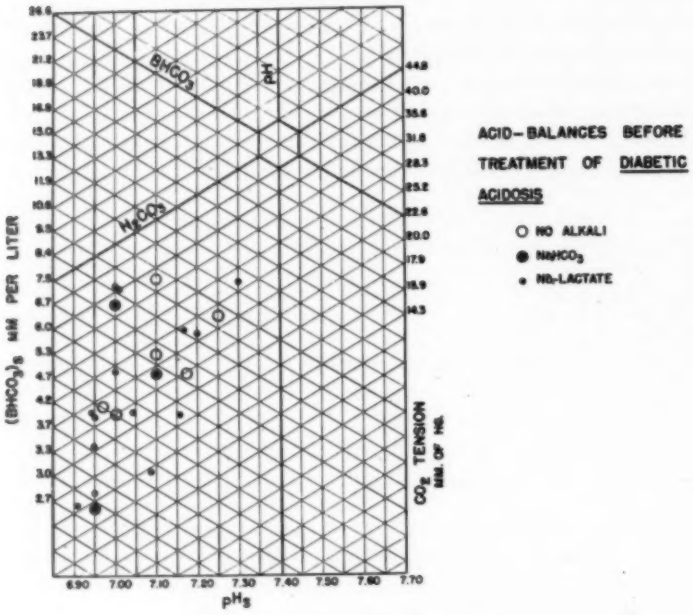
Let us now examine the situation about six hours after treatment with the three different methods.

The six-hour period has been chosen because by this time (1) ketosis significant from the point of view of base-binding no longer exists, (2) all or nearly all of the originally administered fluid has been absorbed, (3) initially administered Na-lactate has been completely metabolized and (4) maximum effect has been obtained from the first dose of insulin. (Figs. 4 and 5.)

We now find that five of the six children receiving *no alkali* have still very poor positions of acid-base balance. In the sixth (No. 5) we had no data at this particular time.

Why have these children done so poorly? Because, we believe (1) their ketosis only partly accounted for their acidosis, (2) much of the fixed base released by oxidation of the ketone acids was claimed by buffer acids other than H_2CO_3, (3) sufficient time had not elapsed for much aid to have been

Fig. 2.


BHCO3
pH
H2CO3
(BHCO3)s MM PER LITER
CO2 TENSION MM. OF HG.
pHs
6.90 7.00 7.10 7.20 7.30 7.40 7.50 7.60 7.70
ACID-BALANCES BEFORE TREATMENT OF DIABETIC ACIDOSIS
NO ALKALI
NaHCO3
Na-LACTATE

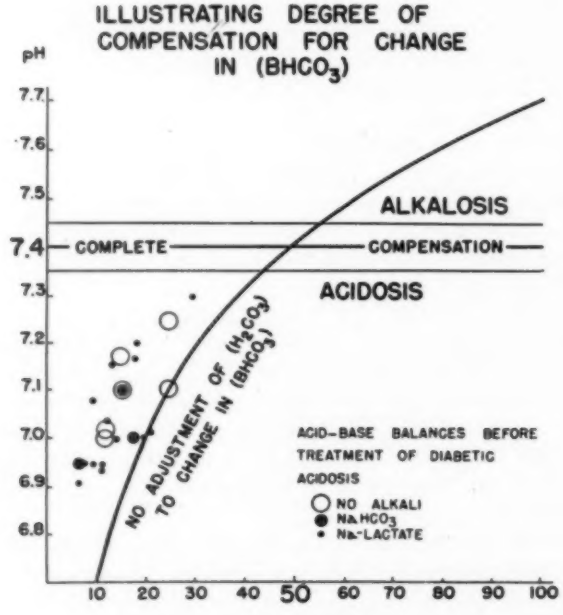
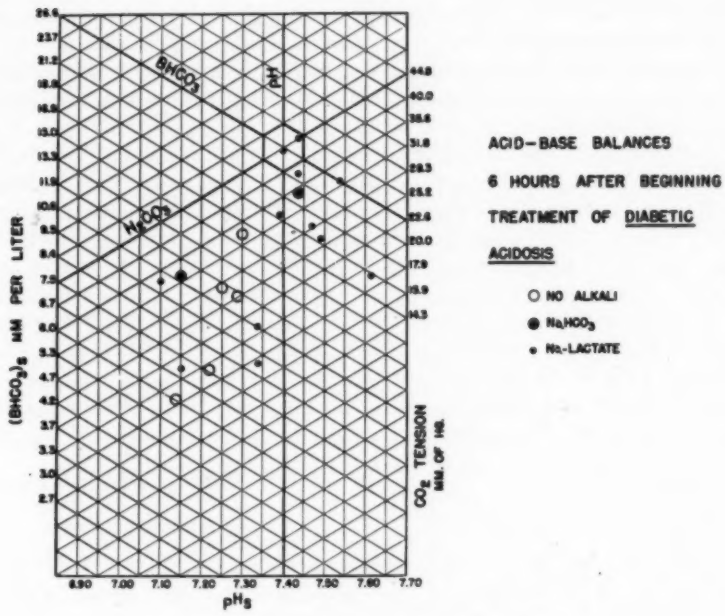

ILLUSTRATING DEGREE OF COMPENSATION FOR CHANGE IN (BHCO3)
pH
7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
6.9
6.8
ALKALOSIS
COMPLETE
COMPENSATION
ACIDOSIS
NO ADJUSTMENT OF (H2CO3) TO CHANGE IN (BHCO3)
ACID-BASE BALANCES BEFORE TREATMENT OF DIABETIC ACIDOSIS
NO ALKALI
NaHCO3
Na-LACTATE
10 20 30 40 50 60 70 80 90 100
PLASMA BICARBONATE, VOL. %

Fig. 3.

Fig. 4.


ACID–BASE BALANCES
6 HOURS AFTER BEGINNING
TREATMENT OF DIABETIC
ACIDOSIS
NO ALKALI
NaHCO3
Na-LACTATE
(BHCO3)s MM PER LITER
pHs
CO2 TENSION
MM. OF HG.

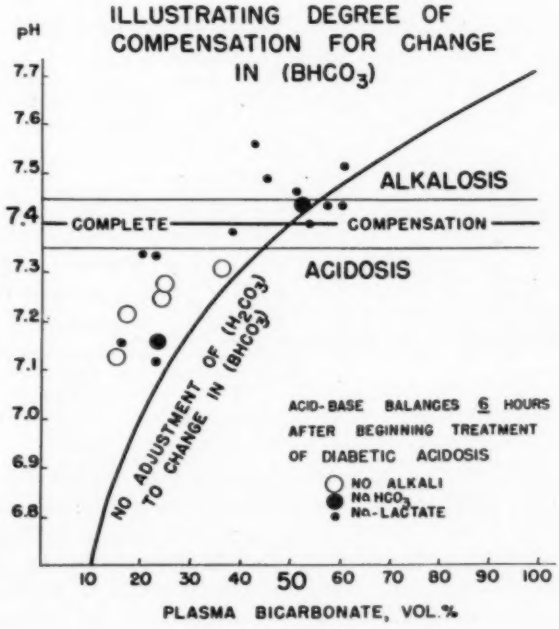

ILLUSTRATING DEGREE OF
COMPENSATION FOR CHANGE
IN (BHCO3)
pH
ALKALOSIS
COMPLETE
COMPENSATION
ACIDOSIS
NO ADJUSTMENT OF (H2CO3)
TO CHANGE IN (BHCO3)
ACID-BASE BALANCES 6 HOURS
AFTER BEGINNING TREATMENT
OF DIABETIC ACIDOSIS
NO ALKALI
NaHCO3
Na-LACTATE
PLASMA BICARBONATE, VOL.%

Fig. 5.

secured by renal excretion of free acid or fixed acid bound to the NH_4 ion, (4) because of restrictions imposed both by time and physical condition, negligible amounts of potential alkali were ingested orally as fruit juices.

One of the three children receiving *$NaHCO_3$* is in normal position (No. 9) eight hours after start of treatment. One (No. 8) is still in poor position after four hours. This patient started with pH_s of 7.00 and ($BHCO_3$) of 10 mM per liter, received the usual amounts of insulin, salt solution, and dextrose and in addition 12 mM/Kg. $NaHCO_3$. Why did he do so poorly? His story is that for almost seven hours after beginning of treatment he remained in circulatory failure, being cyanotic, and with poor pulse. His breathing, while rapid, was not deep. His precarious position was also demonstrated by the remainder of the chemical analysis of his blood taken four hours after the start of treatment, which revealed the fact that the initial lactic acid content of the plasma of 3.7 had increased to *16.2* m.eq. per liter. During the seven- to twenty-one-hour period, improvement was marked, and at the later hour the plasma lactic acid had dropped to 2.5 m.eq. per liter. In the remaining patient receiving $NaHCO_3$ (No. 7) we had no data near the six-hour stage.

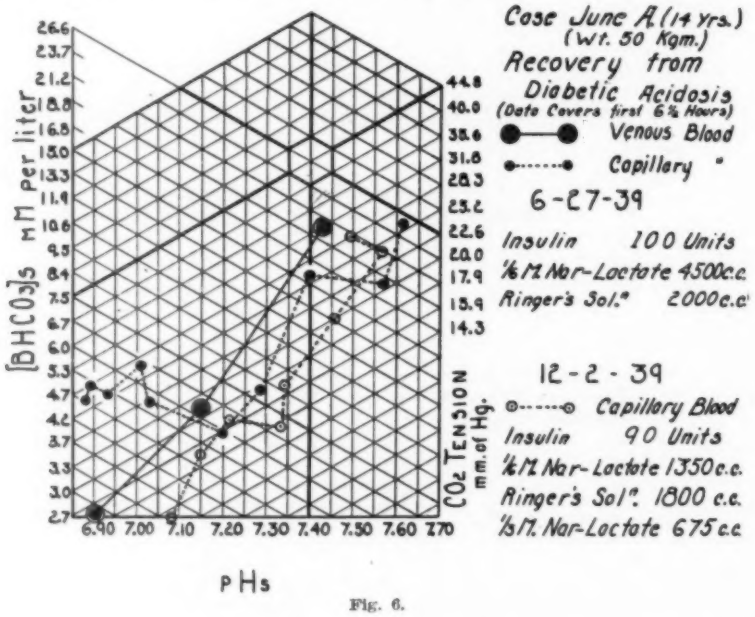


Fig. 6.

Of the twelve Na-lactate-treated patients with data at this time, all but two have made complete or almost complete recovery of pH_s, four somewhat overshooting the mark without, however, showing excessive $BHCO_3$ recovery.

Now let us inquire still more closely into the situation by following some of these patients individually at shorter intervals and for a little longer time. Let us begin with a 14-year-old girl who appears both as Case No. 17 and

No. 18 because in the space of five months she twice required treatment of extreme degrees of acidosis. Data referable to treatment and response are shown in Tables VIII to XI and Fig. 6, inclusive. When seen first, on June 27, 1939 (Fig. 7), her initial acid-base balance is now shown on a different type of chart, where time in hours is recorded on the abscissa, while on the ordinate

TABLE VIII. TREATMENT OF DIABETIC ACIDOSIS: SEVERE DEHYDRATION AND KETOSIS

JUNE A.; AGE 14 YR.; WT. 50 KG.; JUNE 27, 28, 1939		
TIME	TREATMENT	DOSAGE (C.C.)
9:50 A.M.	Insulin HCl, 100 units subcutaneously (before laboratory confirmation)	
9:50 A.M.-11:30 A.M.	"Fortified" Lactate-Ringer's Sol. I.V.	1,500
10:00 A.M.-12:15 P.M.	"Fortified" Lactate-Ringer's Sol. Sub. C.	1,000
12:30 P.M.- 3:40 P.M.	⅙ molar Na r-lactate Sol. I.V.	1,500
3:40 P.M.- 5:00 P.M.	"Fortified" Lactate-Ringer's Sol. I.V.	2,100
9:40 P.M.- 2:00 A.M.	"Fortified" Lactate-Ringer's Sol. Sub. C.	400
Total		6,500

TABLE IX. JUNE A. RECOVERY FROM DIABETIC ACIDOSIS

		CAPILLARY BLOOD					VENOUS BLOOD		
DATE	TIME	Vc%*	pH	CO_{2b}† mM/L.	CO_{2s}‡ mM/L.	CO_{2s} VOL.%	SERUM CO_2 VOL.%	SERUM pH	SERUM TRUE GLUCOSE MG./100 C.C.
6/27/39	9:50 A.M.	48.5	6.88	4.2	4.8	10.9	6.5 (2.9mM)	6.91	448
	10:00 Treatment started								
	10:05	46.5	6.89	4.5	5.2	11.6			
	10:20	45.3	6.93	4.5	5.2	11.6			
	10:35	40.0	7.01	5.7	6.5	14.4			
	10:50	42.2	7.03	4.6	5.5	12.2			
	11:20	41.5	7.05						
	12:15 P.M.						13.9 (6.3mM)	7.15	
	12:20	41.0	7.20	5.1	6.0	13.2			
	1:30	47.0	7.28	6.6	8.0	17.8			
	2:20	51.0	7.40	12.5	15.8	35.2			
	3:25	42.0	7.57	15.1	18.7	41.7			
	3:30								35
6/28/39	4:30	27.5	7.62	22.3	25.7	57.2			
	6:30 A.M.								334
	2:00 P.M.						44.9 (20.2mM)	7.43	207

*Vc = hematocrit.
†CO_{2b} = CO_2 content whole blood in mM/L.
‡CO_{2s} = CO_2 content serum in mM/L.

TABLE X. TREATMENT OF DIABETIC ACIDOSIS
(MODERATE DEHYDRATION, SEVERE (?) KETOSIS)

JUNE A.; AGE 15 YR.; WT. 45 KG.; DEC. 10, 1939		
TIME	TREATMENT	DOSAGE (C.C.)
10:07 A.M.	Insulin HCl, subcutaneously	90 units
10:15 A.M.-11:15 A.M.	⅓ M. Na r-Lactate Sol. intravenously	675
11:15 A.M.- 3:00 P.M.	⅙ M. Na-Lactate Sol. subcutaneously	1,350
	+ Hypotonic Ringer's Sol.	1,800

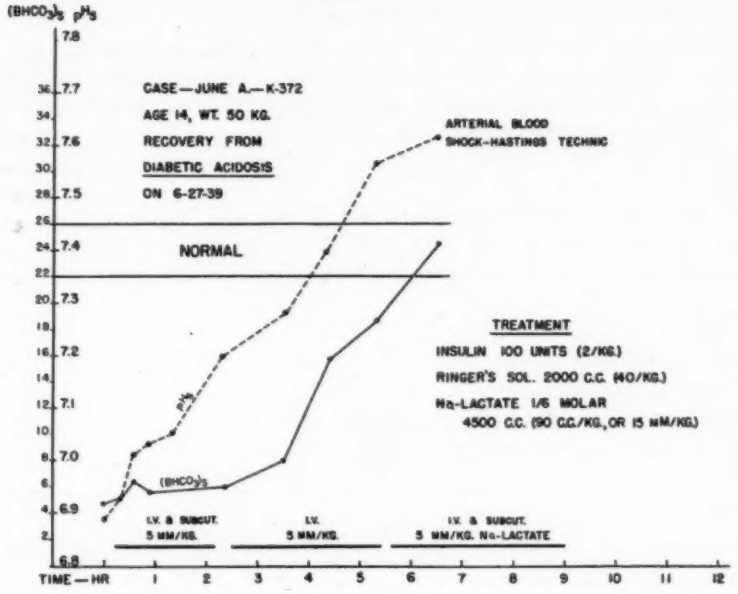
TABLE XI. JUNE A. RECOVERY FROM DIABETIC ACIDOSIS

		CAPILLARY BLOOD					VENOUS BLOOD		
DATE	TIME	Vc%*	pH	CO_{2b}† mM/L.	CO_{2s}‡ mM/L.	CO_{2s} VOL.%	SERUM CO_2 VOL.%	SERUM pH	SERUM TRUE GLUCOSE MG./100 C.C.
12/2/39	9:40 A.M.						11.8 (5.3mM)	7.04	345.0
	9:55	51.0	7.08	2.8	3.4	7.5			
	(10:25 treatment started)	49.0	7.15	4.2	5.0	11.2			
	10:40	45.0	7.22	5.6	6.7	14.9			
	11:00	46.0	7.33	6.1	7.4	16.4			
	11:15	47.0	7.34	7.1	8.7	19.3			
	11:30	44.0	7.46	11.5	14.1	31.4			
	12:35 P.M.	42.5	7.57	13.9	17.3	38.6			
	2:30								44.6
	4:04	42.0	7.49	15.8	19.3	43.1			
	4:30						54.7		
	8:45								

*Vc = hematocrit.
†CO_{2b} = CO_2 content whole blood in mM/L.
‡CO_{2s} = CO_2 content serum in mM/L.

are recorded both pH_s and $(BHCO_3)_s$ on scales so adjusted that coinciding values represent little or no respiratory adjustment of H_2CO_3 for change in $BHCO_3$. Initially, pH_s was 6.91 with $(BHCO_3)_s$ 2.8 mM/L. when determined in venous blood, and pH_s 6.88 and $(BHCO_3)_s$ 4.8 mM/L. when determined by the Shock-Hastings microtechnique in capillary (arterial) blood. Subsequently, by this microtechnique, one of us (J. E.), with the assistance of Mary B. Ruhoff, followed the pathway of acid-base balance recovery in response to the treatment summarized on the chart, the details of which are given in Table VIII. If we examine the nature of recovery closely we will note that during the first two hours there was splendid rise in pH_s (from 6.88 to 7.20), while $(BHCO_3)_s$ was increasing only from 4.8 to 6.0 mM per liter. Such a change as this means that $(H_2CO_3)_s$ had to fall from an initial CO_2 tension of 27 to 16 mm. Hg. This then is what the initial increase in pulmonary ventilation in response to treatment accomplishes. But it also makes it necessary for buffers to bind more base, and in turn this is what largely prevents Na released early from the metabolism of lactate from appearing as $NaHCO_3$, and hence accounts for the early slow increase in $(BHCO_3)_s$. Recovery of $(BHCO_3)_s$ then began to accelerate and soon paralleled that of pH_s. At six hours $(BHCO_3)_s$ was at the average normal value of 24.5 mM/L. while pH_s had overshot to 7.62. As will be noted in subsequent data, such overshooting of pH_s recovery is characteristic of recovery from acidosis. Just as respiratory adjustment of H_2CO_3 falls behind while $BHCO_3$ is diminishing, so also is there failure to adjust immediately to late accelerated $BHCO_3$ recovery. It should be emphasized that no clinical manifestations of CO_2 deficit alkalosis are discernible at this point, although we have felt it wise always to have available 5 per cent CO_2 in oxygen if its administration seemed indicated. Concerning treatment, note

Fig. 7.


(BHCO3)/S pH/S
CASE — JUNE A.— K-372
AGE 14, WT. 50 KG.
RECOVERY FROM
DIABETIC ACIDOSIS
ON 6-27-39
ARTERIAL BLOOD
SHOCK-HASTINGS TECHNIC
NORMAL
TREATMENT
INSULIN 100 UNITS (2/KG.)
RINGER'S SOL. 2000 C.C. (40/KG.)
Na-LACTATE 1/6 MOLAR
4500 C.C. (90 C.C./KG., OR 15 MM/KG.)
pH/S
(BHCO3)/S
I.V. & SUBCUT.
5 MM/KG.
I.V.
5 MM/KG.
I.V. & SUBCUT.
5 MM/KG. Na-LACTATE
TIME — HR

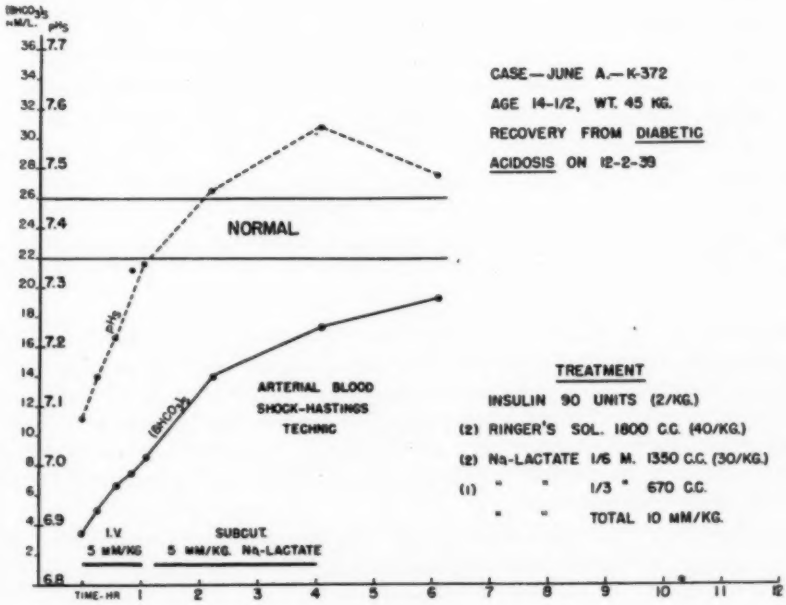

(BHCO3)/S mM/L.
pH/S
CASE — JUNE A.— K-372
AGE 14-1/2, WT. 45 KG.
RECOVERY FROM DIABETIC
ACIDOSIS ON 12-2-39
NORMAL
pH/S
(BHCO3)/S
ARTERIAL BLOOD
SHOCK-HASTINGS
TECHNIC
TREATMENT
INSULIN 90 UNITS (2/KG.)
(2) RINGER'S SOL. 1800 C.C. (40/KG.)
(2) Na-LACTATE 1/6 M. 1350 C.C. (30/KG.)
(1) " " 1/3 " 670 C.C.
" " TOTAL 10 MM/KG.
I.V.
5 MM/KG
SUBCUT.
5 MM/KG. Na-LACTATE
TIME-HR

Fig. 8.

especially in this case that 15 mM Na-lactate per kilogram were required to effect accurate restoration of $(BHCO_3)_s$ in 6½ hours.

When seen a second time, five months later, on Dec. 2, 1939, this girl, while proving to be with even lower initial $(BHCO_3)_s$ (3.4 mM/L.), was much less prostrated and less dehydrated and hyperventilating more than on her previous admission. It was no surprise, therefore, to find her pH_s less reduced, 7.08 (Fig. 8). The pathway of recovery this time varied from the previous one in that both pH_s and $(BHCO_3)_s$ recovered at more rapid rates, but with $(BHCO_3)_s$ again lagging relative to pH_s. At four hours pH_s had overshot to its maximal value of 7.57 with $(BHCO_3)_s$ only 17.3 mM per liter. At six hours, pH_s had dropped to 7.49 while $(BHCO_3)_s$ had reached 19.3 mM per liter.

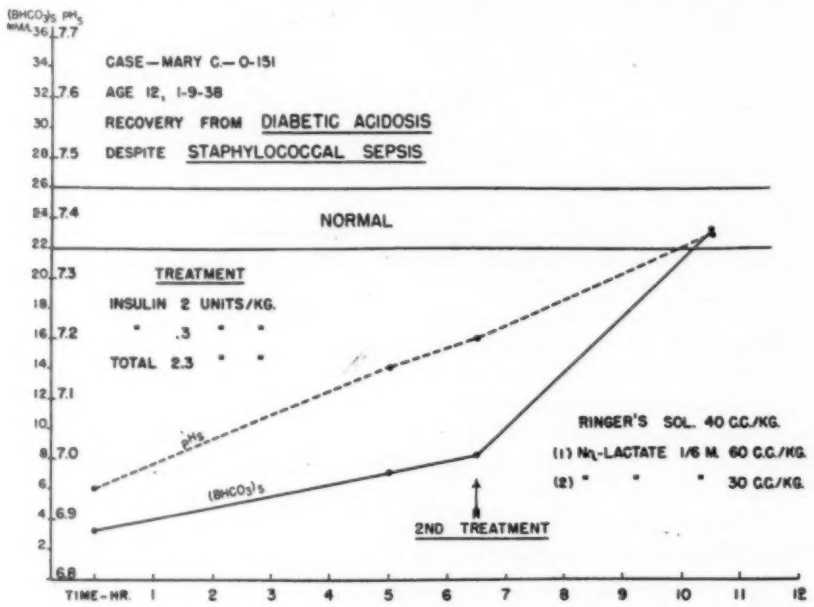
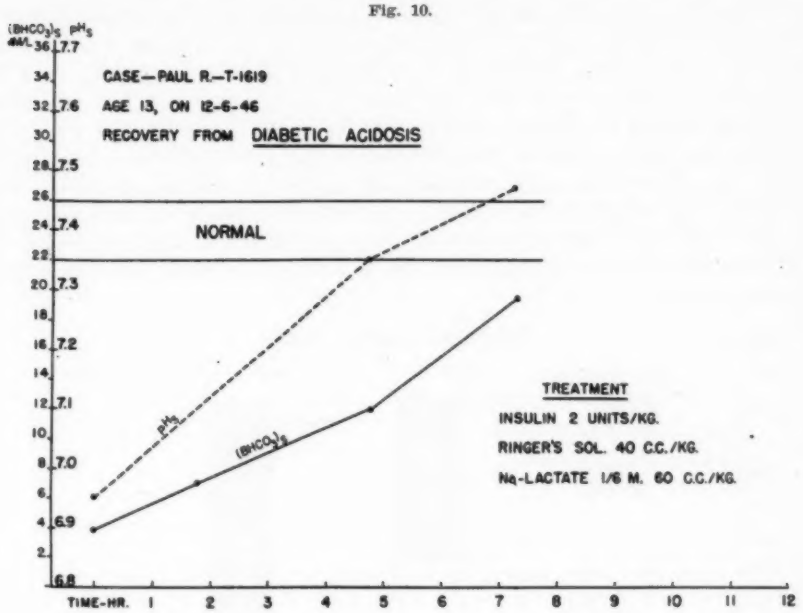


Fig. 9.

Note that in this instance only the initial 10 mM/Kg. of Na-lactate were administered, and while $(BHCO_3)_s$ recovery was not entirely complete in six hours, it was nearly enough so to remove the patient out of all danger and from strain of hyperpnea. Note also that because this patient was initially less dehydrated than usual for a commensurate degree of acidosis, we elected to cut down the total fluid intake by giving half of the Na-lactate in ⅓ molar concentration intravenously.

Case 16, a poorly nourished girl of 12 years, will next be considered (Fig. 9). Moving pictures of this girl will later be shown correlated with the blood chemical data. This subject resembled Case 17 very much on her first admission in that she was in deep coma, very feeble, and with very poor initial

Fig. 10.


(BHCO3)'s pHs
mM/L
CASE—PAUL R.—T-1619
AGE 13, ON 12-6-46
RECOVERY FROM DIABETIC ACIDOSIS
NORMAL
pHs
(BHCO3)'s
TREATMENT
INSULIN 2 UNITS/KG.
RINGER'S SOL. 40 C.C./KG.
Na-LACTATE 1/6 M. 60 C.C./KG.
TIME-HR.

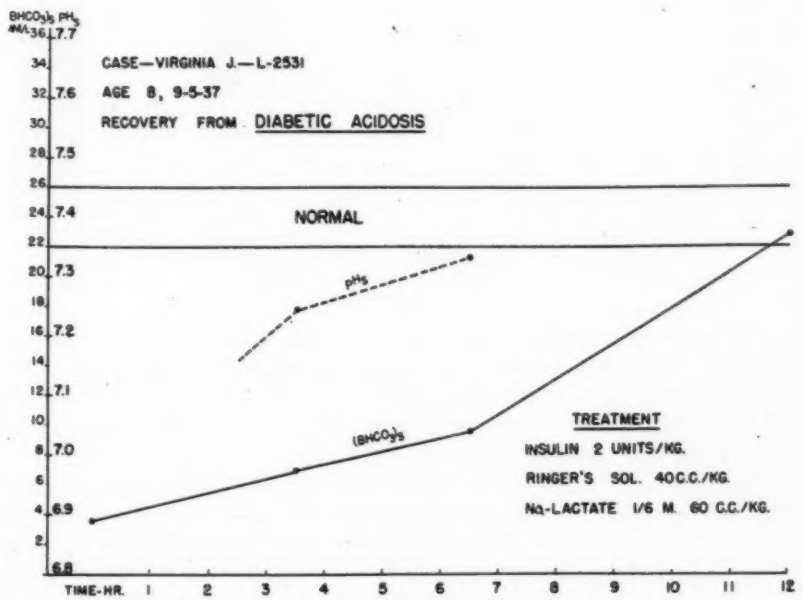

BHCO3's pHs
mM/L
CASE—VIRGINIA J.—L-2531
AGE 8, 9-5-37
RECOVERY FROM DIABETIC ACIDOSIS
NORMAL
pHs
(BHCO3)'s
TREATMENT
INSULIN 2 UNITS/KG.
RINGER'S SOL. 40C.C./KG.
Na-LACTATE 1/6 M. 60 C.C./KG.
TIME-HR.

Fig. 11.

acid-base balance; pH_s 6.95 and $(BHCO_3)_s$ 3.1 mM per liter. In response to the first 10 mM/Kg. dose of Na-lactate, recovery of pH_s was not entirely satisfactory in five hours, from 6.95 to 7.15, and $(BHCO_3)_s$ rose only from 3.1 mM/L. to 7. When these facts were learned and coupled with her still unsatisfactory clinical condition a second dose of 5 mM/Kg. Na-lactate with more insulin was administered at the 6½-hour mark. $(BHCO_3)_s$ recovery then accelerated, and at the ten and one-half hour mark both pH_s and $(BHCO_3)_s$ were normal. The patient by this time had regained complete consciousness and so much strength that she was able to sit up unaided, this in spite of the unsuspected presence of what was the next day to prove to be fatal staphylococcus sepsis.

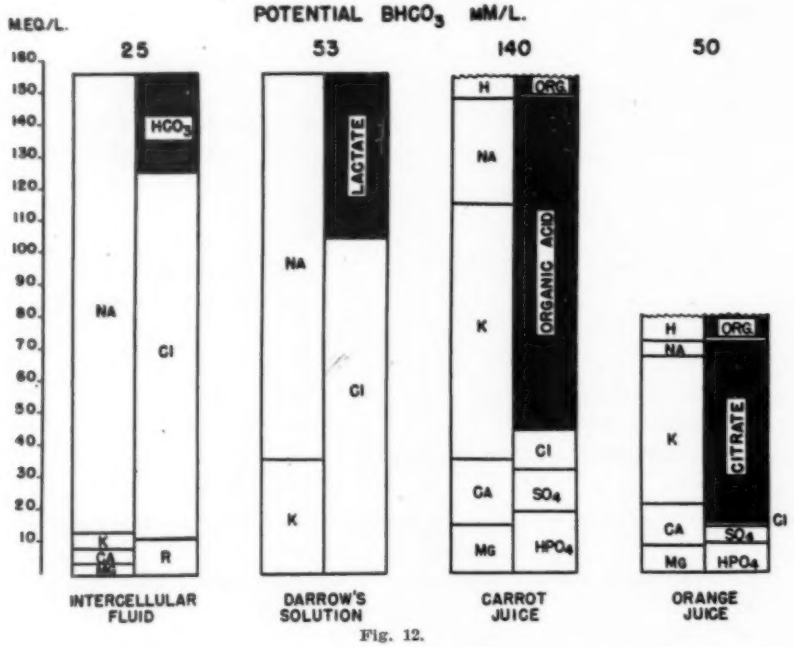
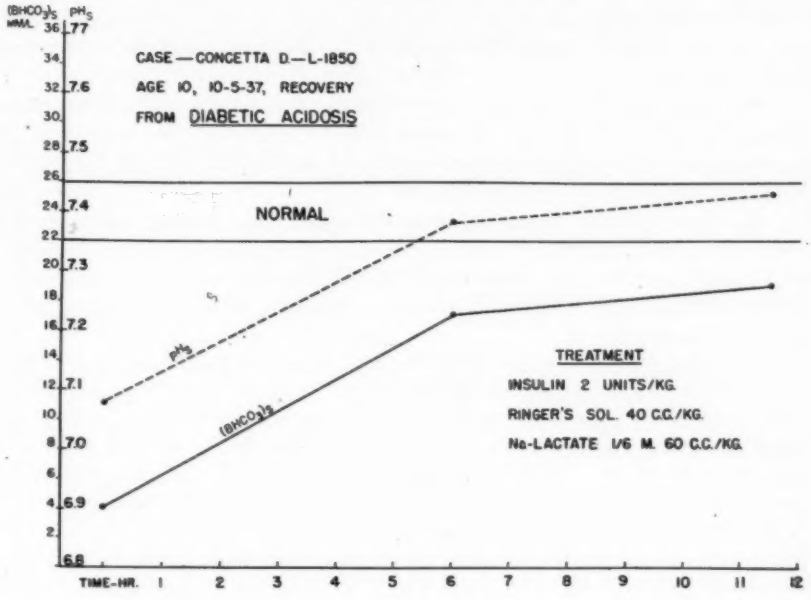


Fig. 12.

The next case (No. 24) a boy aged 13, was admitted Dec. 6, 1946, with quite low $(BHCO_3)_s$, 4 mM/L., and with very poor respiratory adjustment, pH_s of 6.95 (Fig. 10). In response to 10 mM/Kg. Na-lactate he showed in seven hours just what might have been predicted from the previous studies, namely, slight overshooting of pH_s with slight lag of $(BHCO_3)_s$.

In Case 13, a girl aged 8, we lacked an initial pH_s determination to go with the very low initial $(BHCO_3)_s$ of 3.8 mM per liter (Fig. 11). Six and one-half hours after administration of 10 mM/Kg. Na-lactate, pH_s was slightly subnormal, 7.33, while $(BHCO_3)_s$ was only 9.5 mM/L. By the twelve-hour mark, however, $(BHCO_3)_s$ had reached the normal value of 22.8 mM/L., because, undoubtedly, of synergistic and accumulative effects of renal activity, continued insulin

Fig. 13.


(BHCO3)s mM.
pHs
CASE — CONCETTA D.—L-1850
AGE 10, 10-5-37, RECOVERY
FROM DIABETIC ACIDOSIS
NORMAL
pHs
(BHCO3)s
TREATMENT
INSULIN 2 UNITS/KG.
RINGER'S SOL. 40 C.C./KG.
Na-LACTATE 1/6 M. 60 C.C./KG.
TIME-HR.

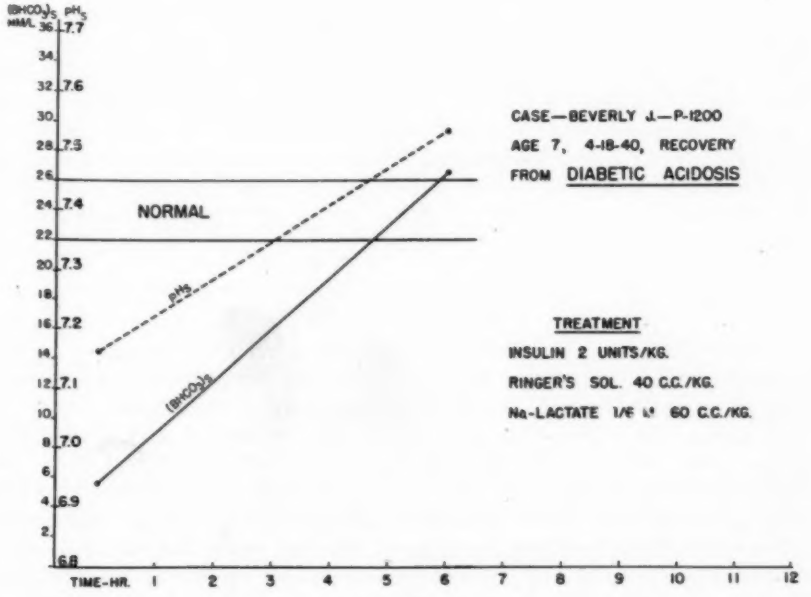

(BHCO3)s mM.
pHs
CASE—BEVERLY J.—P-1200
AGE 7, 4-18-40, RECOVERY
FROM DIABETIC ACIDOSIS
NORMAL
pHs
(BHCO3)s
TREATMENT
INSULIN 2 UNITS/KG.
RINGER'S SOL. 40 C.C./KG.
Na-LACTATE 1/6 M. 60 C.C./KG.
TIME-HR.

Fig. 14.

effect on ketosis, and alkali ingestion in the form of fruit juices. At this point it might be interesting to show what orange juice is when pictured in the way that Gamble first so brilliantly described the chemical anatomy of the body fluids (Fig. 12).

The next case, No. 14, was a girl aged 10 with relatively good respiratory adjustment, pH_a 7.08 for the low initial $(BHCO_3)_a$ of 4 mM per liter (Fig. 13). In response to 10 mM/Kg. Na-lactate, recovery of pH_a and $(BHCO_3)_a$ paralleled each other and were quite satisfactory.

The last case with good follow-up data (Fig. 14), No. 20, a girl aged 11, showed the best respiratory adjustment of all, pH_a 7.16 for initial $(BHCO_3)_a$ of 5.7 mM per liter. In response to 10 mM/Kg. Na-lactate the pathways of recovery of pH_a and $(BHCO_3)_a$ tended to converge, both slightly overshooting at the six-hour mark.

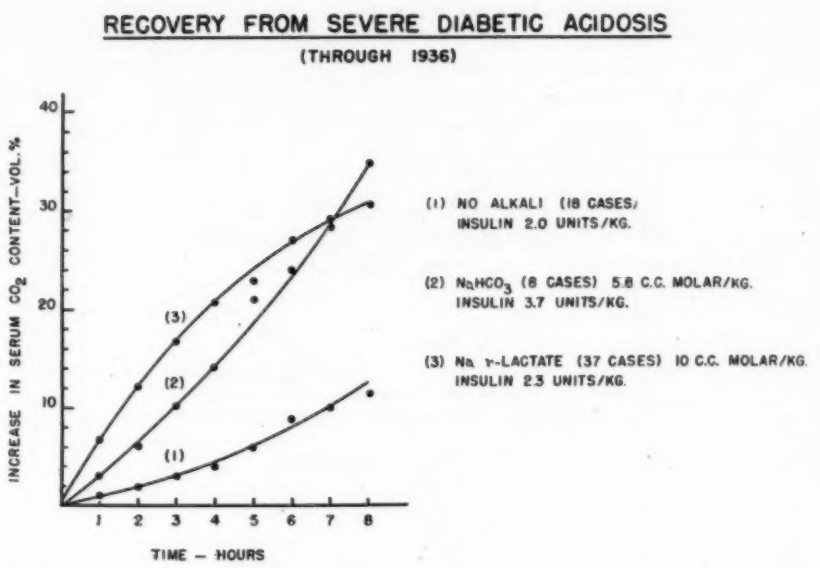
It should be fairly clear from the data presented thus far that the initial serum pH has a predictable influence on the later behavior of serum $BHCO_3$ during recovery. The superiority of our Na-lactate method of therapy as regards speed of recovery from acidosis can be visualized especially well when only recovery of serum $BHCO_3$ is followed during the first eight hours of treatment by the three methods under discussion (Fig. 15) and plotted against time. It will be noted that, on the average, as much is accomplished in two hours with the proper use of Na-lactate as is accomplished in eight hours without alkali administration, and that rise in serum $BHCO_3$ tapers off as the normal value is approached.

Finally, before summarizing the complete series of Na-lactate treated diabetics, we would like to point out another advantage of Na-lactate administration. On three occasions, once in our youngest diabetic of 8 months, and twice in infants of 14 months, we failed to diagnose the type of extreme acidosis with which the infants were brought to the hospital as *diabetic*, and in the early phase of treatment administered 10 mM/Kg. Na-lactate and 40 c.c./Kg. hypotonic Ringer's solution *without any insulin*. Note in Fig. 16 that each was recovering fairly well, in fact much faster than would have been predicted for patients receiving insulin but no alkali, before our error was discovered and insulin administered.

OVER-ALL SUMMARY OF Na-LACTATE TREATED PATIENTS WITH DIABETIC ACIDOSIS

In Table XII we have made an analysis of our entire group of children treated with sodium-lactate. Note that of the 123 treated over a 17-year period ninety-one, or 74 per cent, were either of extreme or severe degree. There were five deaths, all in the group of extreme severity. In no instance did death occur before acidosis was relieved, despite the fact that several lived but a short time after treatment was begun. Two children died from staphylococcus sepsis, one probably from pneumonia, and their deaths seemed unavoidable since they occurred before the days of effective chemotherapy. One death, however, was attended by hyperpyrexia, to which we believe we contributed largely by the administration of hypertonic (molar) Na-lactate despite de-

Fig. 15.


RECOVERY FROM SEVERE DIABETIC ACIDOSIS
(THROUGH 1936)
INCREASE IN SERUM CO_2 CONTENT—VOL. %
40
30
20
10
(3)
(2)
(1)
1 2 3 4 5 6 7 8
TIME — HOURS
(1) NO ALKALI (18 CASES)
INSULIN 2.0 UNITS/KG.
(2) Na_2HCO_3 (8 CASES) 5.8 C.C. MOLAR/KG.
INSULIN 3.7 UNITS/KG.
(3) Na γ-LACTATE (37 CASES) 10 C.C. MOLAR/KG.
INSULIN 2.3 UNITS/KG.

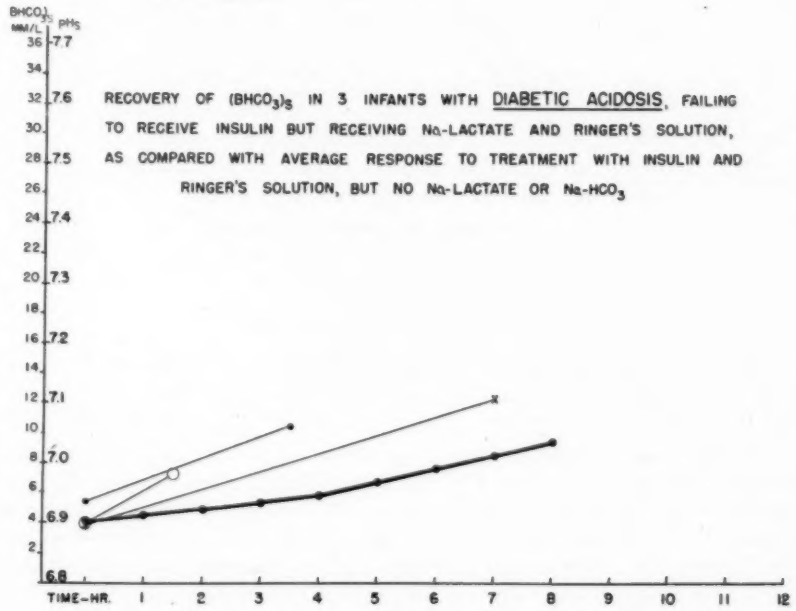

$BHCO_3$ MM/L
pHs
36 7.7
34
32 7.6
30
28 7.5
26
24 7.4
22
20 7.3
18
16 7.2
14
12 7.1
10
8 7.0
6
4 6.9
2
6.8
TIME-HR. 1 2 3 4 5 6 7 8 9 10 11 12
RECOVERY OF $(BHCO_3)_S$ IN 3 INFANTS WITH DIABETIC ACIDOSIS, FAILING TO RECEIVE INSULIN BUT RECEIVING Na-LACTATE AND RINGER'S SOLUTION, AS COMPARED WITH AVERAGE RESPONSE TO TREATMENT WITH INSULIN AND RINGER'S SOLUTION, BUT NO Na-LACTATE OR $Na\text{-}HCO_3$

Fig. 16.

hydration in the presence of already high fever. This was at the very beginning of the studies and has been discussed previously in detail.[14] The fifth death seemed also unnecessary and resulted from cerebral and pulmonary edema following too-rapid administration of too much fluid intravenously.

Because of all these experiences, favorable and unfavorable, we think the details of our treatment are almost as important as the principles, and at the risk of repetition we shall outline them once more in Table XIII.

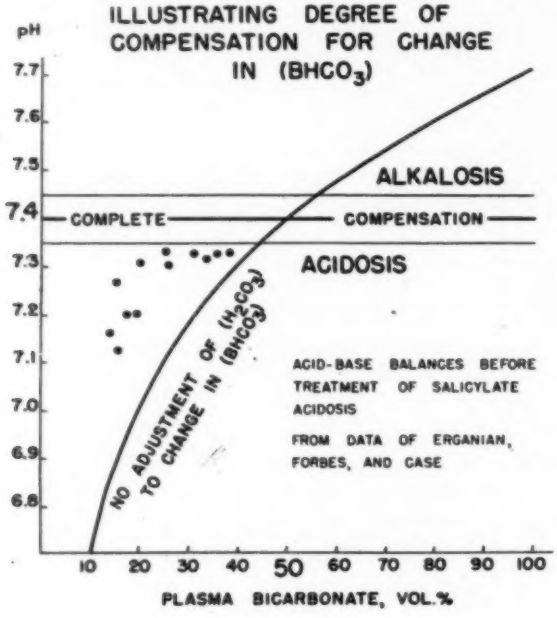


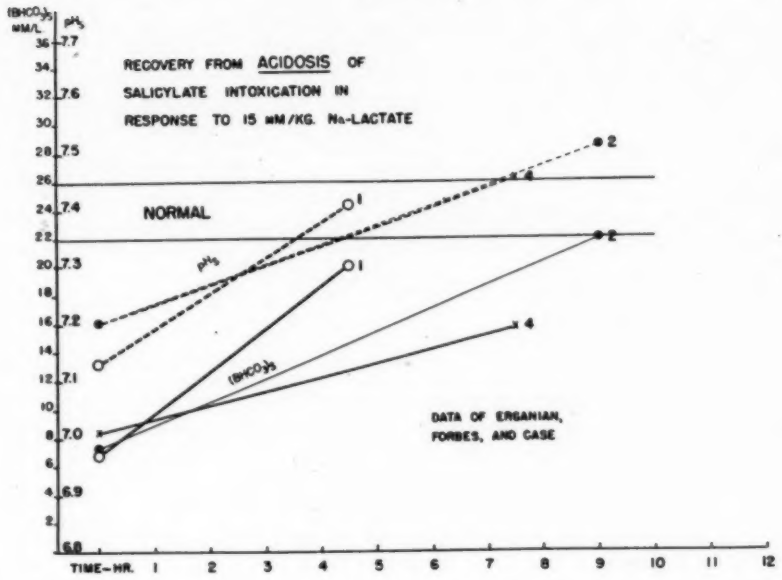
Fig. 17.

NONDIABETIC KETONE ACIDOSIS

Recently there has been an unusual opportunity to study other types of acidosis in which ketosis plays an important role, and a comparison of these with the diabetic is interesting.

In Fig. 17 we have data from twelve subjects, mostly infants, with severe salicylate intoxication. You will note immediately that, as compared with diabetics, their initial acid-base balances are quite good in that respiratory adjustment of $(H_2CO_3)_s$ has prevented much fall of pH_s, despite severe depletion of $(BHCO_3)_s$. The reason is twofold: in the first place, these infants were still strong because they were not seriously ill and were relatively well nourished and not severely dehydrated; in the second place they had a stimulus to respiration even stronger than acidosis—that of salicylate intoxication. The data in these infants were secured by Dr. Jane Erganian, together with Drs.

Fig. 18.


(BHCO3)s mM/L
pHs
RECOVERY FROM ACIDOSIS OF
SALICYLATE INTOXICATION IN
RESPONSE TO 15 mM/KG. Na-LACTATE
NORMAL
pHs
(BHCO3)s
DATA OF ERGANIAN,
FORBES, AND CASE
TIME—HR.

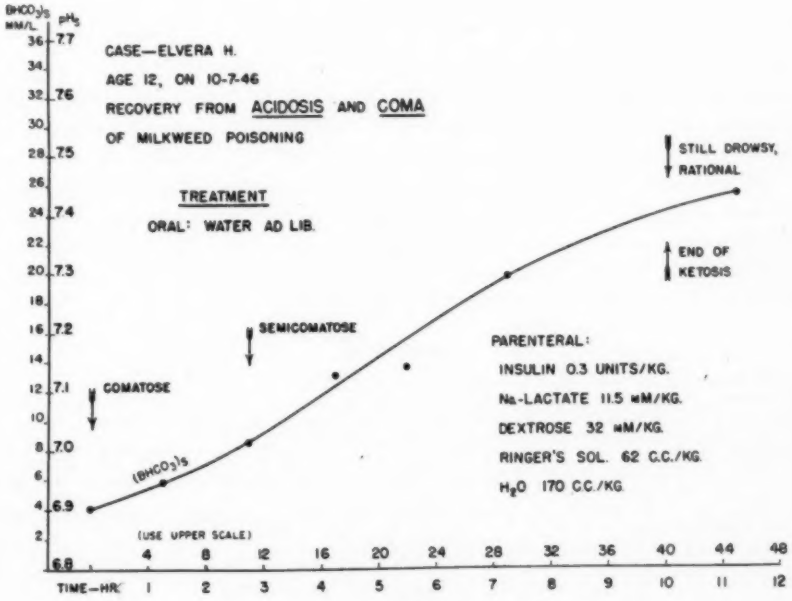

(BHCO3)s mM/L
pHs
CASE—ELVERA H.
AGE 12, ON 10-7-46
RECOVERY FROM ACIDOSIS AND COMA
OF MILKWEED POISONING
TREATMENT
ORAL: WATER AD LIB.
STILL DROWSY, RATIONAL
END OF KETOSIS
SEMICOMATOSE
COMATOSE
PARENTERAL:
INSULIN 0.3 UNITS/KG.
Na-LACTATE 11.5 mM/KG.
DEXTROSE 32 mM/KG.
RINGER'S SOL. 62 C.C./KG.
H2O 170 C.C./KG.
(BHCO3)s
(USE UPPER SCALE)
TIME—HR.

Fig. 19.

TABLE XII. RESULTS IN DIABETIC ACIDOSIS TREATED WITH NA-LACTATE (1930-1946 INCLUSIVE, 123 CASES)

DEGREE ACIDOSIS	RECOVERED	DIED
Extreme acidosis (CO_2 cont. 6-14.9 vol. %) ($BHCO_3$ 2.5-6.3 mM/L.)	48	5 *Cause of death* Hyperpyrexia (1930) Pneumonia ? (1931) Staph. sepsis (1935) Staph. sepsis (1938) Water intoxication (1938)
Severe acidosis (CO_2 cont. 15-24.9 vol. %) ($BHCO_3$ 6.4-10.6 mM/L.)	43	0
Moderate acidosis (CO_2 cont. 25-34.9 vol. %) ($BHCO_3$ 10.7-14.8 mM/L.)	23	0
Mild acidosis (CO_2 cont. 35-44.9 vol. %) ($BHCO_3$ 14.9-19.1 mM/L.)	9	0

TABLE XIII. TREATMENT OF SEVERE DIABETIC ACIDOSIS

Initial
1. Insulin—2 units/Kg.
2. I.V. ⅙ M. Na-lactate—30 c.c./Kg. or 5 mM/Kg.
3. Subcutaneous ⅙ M. Na-lactate—30 c.c./Kg. or 5 mM/Kg.
4. \+ Hypotonic Ringer's—40 c.c./Kg. or 4 m.eq. Cl/Kg.

At 6 Hours
1. Insulin—½ ± unit/Kg.
2. More subcutaneous ⅙ M. Na-lactate if necessary—5 mM/Kg.
3. Plasma, concentrated albumen or whole blood if necessary

Forbes and Case and previously reported,[25] and in Fig. 18 are shown the recoveries of the three infants requiring the largest dose of Na-lactate, 15 mM/Kg. Note that recovery of pH_s parallels that of $(BHCO_3)_s$, but that, considering the dose of alkali administered, the *rate* of recovery of each is relatively slow.

Still slower is the recovery from milkweed poisoning (Fig. 19). Note that the time scale had to be changed fourfold. In this type of poisoning, as in salicylate intoxication, ketogenesis does not cease with insulin administration as in diabetes, but may persist for several days, despite much glucose administration which is indicated along with Na-lactate.

REFERENCES

1. Hartmann, A. F.: M. Clin. North America 9: 1, 1925.
2. Gamble, J. L.: New Eng. J. Med. 201: 909, 1929.
3. Hoag, L. A., and Marples, E.: Proc. Soc. Exper. Biol. & Med. 26: 374, 1929.
4. Hoag, L. A., and Marples, E.: Am. J. Dis. Child. 42: 291, 1931.
5. Joslin, E. P., Root, H. P., White, P., and Marble, A.: J. A. M. A. 105: 359, 1935.
6. Joslin, E. P., Root, H. P., White, P., Marble, A., and Joslin, A. P.: Arch. Int. Med. 59: 175, 1937.
7. Peters, J. P., Bulger, H. A., Eiseman, A. J., and Lee, C.: J. Clin. Investigation 2: 167, 1925.
8. Hartmann, A. F.: Am. J. Dis. Child. 25: 557, 1928.
9. Hartmann, A. F., and Darrow, D. C.: J. Clin. Investigation 6: 257, 1928.
10. Hartmann, A. F., and Elman, R.: J. Exper. Med. 50: 387, 1929.
11. Hartmann, A. F.: Colorado Med. 26: 373, 1929.
12. Hartmann, A. F., and Senn, M. J. E.: J. Clin. Investigation 11: 337, 1932.
13. Marriott, W. McK., Hartmann, A. F., and Senn, M. J. E.: J. PEDIAT. 111: 181, 1933.

14. Hartmann, A. F., Perley, A. M., Basman, J., Nelson, M. V., and Asher, C.: J. PEDIAT. 13: 692, 1938.
15. Hartmann, A. F.: Student Notes on Parenteral Fluid Administration, 1940.
16. Hartmann, A. F.: Washington University Medical Alumni Quarterly, Oct., 1942.
17. Hartmann, A. F., Lawler, H. J., and Meeker, C. S.: J. PEDIAT. 24: 371, 1944.
18. Butler, A. M., and Talbot, N. B.: New Eng. J. Med. 231: 585, 1944.
19. Levine, S. Z.: J. PEDIAT. 26: 196, 1945.
20. Weihl, C., Rapoport, S., and Dodd, K.: J. PEDIAT. 30: 45, 1947.
21. Darrow, D. C.: J. PEDIAT. 28: 515, 1946.
22. Peters and Van Slyke: Quantitative Clinical Chemistry, Baltimore, 1931, Williams and Wilkins Co., p. 894.
23. Hastings, A. B., and Steinhaus, A. H.: Am. J. Physiol. 96: 538, 1931.
24. Gamble, J. L.: Chemical Anatomy, Physiology and Pathology of Extracellular Fluids. Dep't of Pediatrics, Harvard Medical School, 1941. Chart 10.
25. Erganian, J. A., Forbes, G. B., and Case, D. M.: J. PEDIAT. 30: 129, 1947.

STUTTERING, A REORIENTATION

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STUTTERING, in spite of the wealth of published matter that has accumulated, is still one of the most controversial and misunderstood problems which confronts the pediatrician. There are now over one million stutterers in the United States. This large group of persons merits our persistent efforts at better understanding, since their handicap is a continuous source of suffering to them. Van Riper[1] states that seven times as many stutterers contemplate suicide as normal speakers. Adult stutterers tend to go into vocations far below their capacities in order to avoid speaking situations. They often lead misshapen, unhappy lives because of their speech difficulty.

Because the literature until recently has been so contradictory, the physician often dealt with the stuttering child by telling the mother one of two things: that the child would outgrow his speech trouble or that the problem should wait until the child attained school age, at which time he could be enrolled in a speech correction class. Neither suggestion deals with the basis of the child's difficulty. Experience has shown that only those children "outgrow" stuttering whose environmental tensions are eased, purposely or accidentally. A group speech correction class for a child merely concentrates his attention on his defect and does not remove the underlying emotional causes of it. The purpose of this paper is to bring together some of the more recent advances in the understanding of stuttering and to present a point of view which attends more to the child who is saddled with the speech difficulty than to the difficulty itself.

Whereas stuttering has been described at various times as caused by "transient auditory amnesia" (Bluemel[2]), "diminution of the power of visualization" (Swift[3]), and "lack of development of a dominant cerebral hemisphere" (Travis),[4] the majority of workers now agree that stuttering is essentially functional or psychogenic in origin. Two observations strongly support the latter view. The first is that if preschool children are relieved of the distressing emotional tensions of their environment, their stuttering ceases even though no attention, professional or otherwise, has been given to their speech. The second observation is that in primitive cultures where there are no pressures put on children to speak correctly, there are no stutterers.

Johnson[5] found that he could help three out of four preschool children to regain normal speech by directing his total therapeutic efforts to the attitudes of parents and the other adults influencing the child. Johnson reported, "The children are not talked to about their speech, nor are they given instructions as to how they should speak. Treatment was directed to the semantic environment. An attempt was made to change parental attitudes and policies, so that an environment would be formed in which there would be a minimum of anxiety, tension, and disapproval. The parents were to let the child know his speech was

approved regardless of how he spoke. Another measure was to bring about a more friendly relationship between parents and their child. Their tendency to be critical and disapproving tended to make for generally strained relations and for apparent feelings of insecurity on the part of the child.

"In general, then, the treatment is to be directed not toward the child, but toward the relevant evaluations—the attitudes, assumptions, beliefs, etc., and the resulting policies and reactions of the child's parents and teachers and other persons who affect his own evaluations and reactions."

Primitive peoples do not have the problem of stuttering. Harriett Hayes,[5] a teacher on an Indian reservation in Idaho, was unable to find any stuttering Indians. Their standards of child care and training appeared to be extraordinarily lax in comparison with our own. Particularly in regard to speech, it seemed that every Indian child was considered a satisfactory or normal speaker regardless of the manner in which he spoke. Helen Bradley[6] of the U. S. Indian School at Albuquerque, New Mexico, reported that she had never seen a case of stuttering in her school. Margaret Mead[6] commented, "I have never seen stuttering among any of the primitive peoples whom I have studied." Dr. Lloyd C. Warner[6] said that there were no cases in any of the Australian tribes which he had studied. Surely if the causes for stuttering were organic and not functional, it would be found among all peoples, and it would be refractory to the treatment of manipulating the parental attitudes affecting the preschool child.

Despert[7] and Johnson[8] have shown that children begin to stutter between the ages of 2 and 4. At this time they are not only learning to speak in sentences, but they are mastering the art of feeding themselves and are bringing the complex functions of urination and defecation under voluntary control. This is the so-called "period of resistance," at which time the emerging egos of children declare their independence. In this same period many parents are obsessively anxious over the correct "habit training," weight gain, and other developmental phenomena of their children. Conflicts arise between children who are learning, among other things, how to say no, and adults who are desperately trying to "mold" their charges to some preconceived pattern.

As for speech, the vocabulary of preschool children increases several hundred per cent in the space of a few months. In their groping and repeating in an effort to express themselves, they all do some of those things which in adults we characterize as stuttering. Davis[9] has demonstrated that hesitating, repetitious speech is more or less characteristic of young children generally. The development of normal speech will proceed if this 2- to 4-year period is relatively free of emotional tensions. However, if the emotional upheaval in the home is considerable, the child's resultant insecurity feelings may manifest themselves in stuttering. Correcting his speech, interrupting him, and telling him to speak more slowly only focus more of his attention on his speech, augment his feelings of insecurity, and aggravate his speech difficulty.

Later on, the school-age child's stuttering begins to prevent his social adaptation, thereby increasing his anxiety and further fixating his speech trouble. Usually, by the time he is 7 years old, the opportunity has been lost

to help the child's speech by merely easing the emotional tensions within his home. The problem then becomes more complex because the child has internalized much of the environmental conflict surrounding him. A pluralistic therapy which combines direct speech training, skilled individualized psychotherapy, and environmental manipulation becomes necessary for the stuttering school child.

We have emphasized that stuttering is a psychogenic disorder developing in a matrix of emotional tensions during the child's speech development period from 2 to 4 years of age. It follows, then, that the actual causes of stuttering are highly individual, since the causes of tensions differ with each family constellation. Because the underlying causes for each child's speech trouble are so highly individualized, their understanding is sometimes obscured by lumping "cases" together for various statistical purposes. But there are certain facts which can be obtained in no other way. Some of these are:

1. Stuttering is more common in boys than in girls. The ratio varies with the authority from 3:1 to 8:1.

2. Stutterers do poorly on the Ozeretsky Tests for motor coordination (Kopp),[11] but their coordination improves after psychotherapy (Despert).[7]

3. Stuttering appears and disappears with changes in the social environment and in conversational relationships in which the patient is involved (West).[12]

4. Each child has his own individual stuttering pattern.

5. When alone, when singing, and when reading in unison with others, a large number of stutterers speak fluently.

There are certain tension producing factors in the environment of these children that recur with sufficient frequency to deserve special mention.

1. The mothers of stutterers are commonly found to be domineering, perfectionistic, overprotective mothers who are overanxious about the feeding and health of their child. In a recent study, Despert[10] reported that 36 out of 50 mothers of stuttering children were of this type. Such mothers create in their children an excessive amount of restlessness by their anxious coercion, especially during meals, and they inhibit their children's motor activity by an overprotective concern for their health and safety.

2. Overanxiety about the normally repetitive speech of small children is often present in the family background of stutterers. Many parents, especially those who have stuttered, become unduly anxious because of these normal repetitions. As far as a stutterer is concerned, there is nothing more horrible than stuttering. So he corrects his child, tells him to go slowly, to think before he speaks, etc. The child, in consciously attempting to control his speech, stutters even more. So common is this concern over normal repetition that Johnson[8] has spoken of stuttering as a "diagnosogenic" disorder in the sense that the diagnosis of stuttering in a young child by parents and the subsequent attempts on their part to correct his speech is one of the causes of the disorder.

The following cases demonstrate some of the emotional factors in the background of our stuttering children.

CARL A. was a blonde, physically healthy, neatly dressed 7-year-old boy who was brought into The Children's Psychiatric Service of the Harriet Lane Home for Invalid Children, The Johns Hopkins Hospital, by his mother because of stuttering which had started before his entrance into kindergarten. His mother said that he was always "lazy" in his speech. Up until the age of 4 he said very little, but pointed to objects in order to make his wishes known. He began to stutter before he started school, but in the past year his stuttering had become much worse. He wasn't interested in his second-grade studies and his teacher had very little patience with him. His mother expressed this attitude:

"He doesn't seem to care that he stutters. I get after him quite a bit about it, but he doesn't care. I've corrected him about it more in the past year, but it hasn't done any good. He doesn't concentrate. When I help him with his schoolwork he just doesn't seem to think. I go over and over his homework with him, but it doesn't help. I told him that if he doesn't get his lessons he won't get to play in the afternoon after school.

"He eats and sleeps well. He occasionally wets the bed. Nothing seems to worry him. You have to come right down on him to make him do things. I have to wash his face and comb his hair. He cries easily."

Carl's mother was a tense, tearful woman of 40 years who worked as a stenographer after graduating from high school. She had always been lame, the result of an attack of infantile paralysis when she was a child. She kept her stenographic job even after she was married because she felt her husband was too independable to carry the financial responsibility for the family.

Carl's father was a talkative, superficially gay, 40-year-old carpenter, who drank heavily in his youth, but who had reformed at his wife's insistence after marriage. He spent much of his time trying to invent gadgets and resented his wife's disgust at his inventions even though none of them had ever been marketed. He was an irritable, impatient man who scolded Carl some, but mostly ignored him.

Carl's birth and early development were normal except for his delayed speech. Until the age of 4 he was cared for mostly by his maternal grandmother, a warm, permissive individual who loved him devotedly. Shortly after her death his stuttering began. At the time he was first seen in the clinic he was a neat, attractive, serious, somewhat shy boy who spoke in a halting manner, blocking markedly at the beginning of each sentence. His explosive speech was accompanied by a variety of facial grimaces. In spite of his speech difficulty he cooperated well on the Binet examination, attaining a mental age of 6 years, 10 months with an I.Q. of 95. He was right-handed, right-footed and right-eyed.

Stuttering, then, began to be a problem with Carl at the age of 4, shortly after the death of his beloved grandmother. His mother, a tense, coercive woman, worked during the day and spent the little time she had with him at night in pushing and correcting him. His easily irritated, impractical father seldom saw the boy, as his work and hobbies kept him occupied far into the night. The loving support in Carl's environment was terminated by the death of his grandmother at the time he was struggling to bring his speech mechanism under control. For the preceding three years the boy had been deprived of needed affection and had been coerced and criticized, particularly in the areas of speech, schoolwork, and cleanliness.

Improvement is taking place very slowly in Carl because the parental attitudes in this case are so difficult to modify. He is being seen by P. J. Glasner, speech therapist, and a broad program of speech correction, psychotherapy and work with the boy's parents is being followed.

ROBERT C., a 10-year, 3-month-old boy, was brought to the clinic by his mother because of stuttering, obesity, and enuresis. His mother, an obese, restless woman, gave this story.

"It's his nerves I guess that cause the defect in his speech. He has had this since he was about 3 years old. He screws up his mouth to the side and he can't get the words out. He wets the bed. He is overweight. The doctor put him on a diet, but it's so hard to put a child on a diet.

"He is a very good child, and jolly. When he was little the other boys did pick on him, but I always stepped in and tried to find out why. When he was 3 years old I went to the

hospital for seven weeks and after that he started to stutter. He is always so afraid I'm going to leave him. He bites his nails terribly."

This mother kept stopping the boy in speaking situations in an effort to correct his stuttering. She was overconcerned about his keeping neat and clean, and at the time of his admission to the clinic she was still dressing him. She always gave him anything he wanted and was continually fearful that he would get hurt. She would not let him ride streetcars alone and insisted that he hold her hand when they crossed streets.

Mrs. C. is a 33-year-old woman who, after high school, worked for eight years as a clerk in a department store. She was tense, obese, and subject to crying spells.

Mr. C. was a policeman. An impatient man, subject to anger outbursts, he was stern with the boy and frequently quarreled with his wife over the boy's discipline.

Robert was an only child. He was prematurely delivered by cesarean section and weighed only 3 pounds at birth. However, his early development was normal. He did average work in school and behaved very well. His I.Q. was 107. He was right-handed, right-footed and left-eyed.

This boy was prematurely born, so that a great amount of attention was focused on him in infancy. He was the only son of an unstable, fearful, overprotective mother and a stern, easily angered father. In addition to the insecurity this boy felt because of his mother's anxious overprotection and the parental arguments about his discipline, he was constantly cautioned about keeping neat and clean, about speaking correctly and about not overeating.

This boy also had a full program of psychotherapy and speech correction and his parents were frequently seen in order to bring about a healthier relationship between parents and child. Robert has responded to these efforts by speaking without suttering, by losing 20 lbs. of excess weight, and by stopping his enuresis. The satisfactory solution of this problem took almost two years of weekly interviews to accomplish.

CONCLUSIONS

The literature on stuttering is controversial, but most authorities now agree that it is a functional or psychogenic disorder rather than an organic one.

Stuttering begins between the ages of 2 to 4, and departs from normal childhood repetitious speech as a result of insecurity feelings engendered by emotional tensions within the home environment.

Some of the more common factors causing these emotional tensions are listed.

Preschool children can be helped by treatment directed to the adult environment surrounding them. The correction of faulty parental attitudes and the easing of environmental tensions are often all that is needed for them to regain normal speech.

Speech correction classes at school, which attempts to teach stutterers as a group, focuses more attention on the child's defective speech while ignoring the individual emotional causes of it, and thus tends to aggravate the speech difficulty.

School children, especially those 7 years of age or older, need a more thorough therapeutic regimen, including speech training, individualized psychotherapy, and environmental manipulation in order to cope adequately with their more complex problem.

In the light of our recently acquired insight, then, the pediatrician will think of his young patient's stuttering as a symptom of an underlying emotional disturbance, just as he thinks of fever as an indication of an underlying infection. He will seek the causes of this inner unrest by investigating the attitudes

of the adults surrounding his patient, and direct his therapeutic efforts to them. For his older children he will inquire into the methods of the near-by speech instructors, to see if they have the training and understanding to be competent psychotherapists as well as speech technicians. He will realize that a therapeutic program which is not individualized or which does not attempt to understand the child's emotional difficulties makes the child more conscious than ever of his defective speech and does him more harm than good.

REFERENCES

1. Van Riper, Charles: The Nature of Stuttering, Dept. of Speech, Western State Teachers College.
2. Bluemel, C. S.: Stammering and Allied Disorders, New York, 1935, The Macmillan Company.
3. Swift, W. B.: Visualization Is the Best Method for Stammering, Proc. Am. Soc. Study Disorders Speech, 1930, p. 83.
4. Travis, L. E.: Speech Pathology, New York, 1931, D. Appleton-Century Company, Inc.
5. Johnson, Wendell: The Indians Have No Word for It: I. Stuttering in Children, Quarterly J. Speech **30:** 330, 1945.
6. Bullen, A. K.: A Cross-Cultural Approach to the Problem of Stuttering, Child Development **16:** 1, 1945.
7. Despert, J. Louise: A Therapeutic Approach to the Problem of Stuttering in Children, Nervous Child **2:** 2, 1943.
8. Johnson, Wendell: A Study of the Onset and Development of Stuttering. Speech Disorders **7:** 251, 1942.
9. Davis, Dorothy M.: The Relation of Repetitions of the Speech of Young Children to Certain Measures of Language Maturity and Situational Factors, J. Speech Disorders **4:** 308, 1939.
10. Despert, J. Louise: Psychosomatic Study of Fifty Stuttering Children, Am. J. Orthopsychiatry **16:** 100, 1946.
11. Kopp, Helene: Ozeretzky Tests, Am. Orthopsychiatry **16:** 114, 1946.
12. West, Robert: The Pathology of Stuttering, The Nervous Child **2:** 96, 1943.
13. Karlin, I. W., and Kennedy, L.: Stuttering—Problem and Suggested Treatment, Am. J. Dis. Child. **55:** 383, 1938.

EPIDEMIOLOGIC STUDIES IN DENTAL CARIES

II. The Incidence of Caries Among Institutionalized Children

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THE incidence and extent of tooth decay among children cannot be clearly defined by a simple statement of an average value. Dental caries is inconstant as to incidence and rate of progression, not only for the whole child population but for a given child from one period to another.[1] With regimentation of certain conditions of living, however, there tends to less variability of caries experience. Recognizing this fact, and as a means of approach to the study of the possible effect of specific factors on caries evolution, one may gain valuable information from the manner in which caries manifests itself within various defined child populations. The extensive studies of the children of Hagerstown, Md., conducted by members of the United States Public Health Service, provide a reliable source of reference concerning a specified general school population.[2] For several years, similar studies have been under way at the State University of Iowa under the joint sponsorship of the Departments of Pediatrics and Pedodontics, of the Colleges of Medicine and Dentistry. The first report of the present series dealt with the caries course of children seen recurrently in the Children's Clinic of the Dental College.[1] The current report is based on the analysis of dental data from children living in six custodial institutions in the State of Iowa. The data have been analyzed to permit study of the possible effect of certain factors on the dental caries picture. These factors included the sex and age of the subject, the particular institution in which he lived, the duration of residence there, recent exposure to fluorine ingestion, dental hygienic practices, the extent of reparative dental therapy, and conditions of environment which were common or peculiar to specific institutions.

The current study was begun in the summer of 1944, and certain phases of the findings have been reported.[3] The earlier data were supplemented during the summer of 1946 through examinations made in a school for the feeble-minded. The assembled data from all of the institutions include records of 619 children between the ages of 6 and 19 years (Table I). The subject population was not evenly divided between the various institutions, nor was the age distribution equal. Of the subjects, 15 per cent were in the first decade of life; more than one-half were 14 years old or older. The institutions included two orphanages, an industrial school for boys, and a school for the feeble-minded, all populous and under state control; also included were two small Catholic orphanages. The latter two institutions contributed only 10 per cent of the total child population with an age range limited principally from 8 to 13 years.

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Because of this inequality of age and number of subjects in the different institutions, the data in some of the tables accompanying this report have been limited to certain groups of subjects; in other tables the data for certain subgroups have been pooled so as to form homogeneous groups appropriate as to age and number for the analysis under consideration. In no instance has such limitation or pooling of subjects led to perversion of the general trends of the data. Statistically considered, the greatest reliability of data lies in the groups from the state institutions, particularly among those from 14 to 19 years of age.

PRESENTATION OF DATA

The incidence of caries in permanent teeth has been summarized in Tables II to V inclusive. For each subgroup studied, the data include the mean or median value for caries incidence, the total range of observed values, and the range for the middle one-half of the subjects. As a measure of caries extent we have used the number of surfaces of permanent teeth which have shown decay in each subject's mouth. The symbol DMF is used to connote decayed, missing, or filled: each extracted tooth is considered to have had three carious surfaces prior to extraction. The basis for this assumption will be given consideration in the discussion of results.

Table II deals with all subjects in terms of age, without regard to sex, place, or duration of residence. Table III presents the data in terms of the specific custodial institution. Table IV deals with the caries scores differentiated according to sex. Table V provides correlation of caries experience with the respective duration of residence under custodial regimentation.

The median caries extent was progressively greater in each successive age group (Table II), with an increment approximating one newly affected tooth surface each year. It is worthy of comment that no acceleration of caries progression rate was evident during the postshedding years. Only the school for the feeble-minded provided sufficient numbers of subjects to permit comparison of caries incidence among its subjects for the full age range of this study. In that institution, the median caries values during the early, late, and postshedding periods (6 to 9, 10 to 13, and 14 to 19 years of age) were four, six, and eight affected tooth surfaces, respectively. Among the various institutions, the median values for affected surfaces among those 14 to 19 years old ranged from the low of eight surfaces for the feeble-minded group to fourteen surfaces for the boys from the industrial school (Table III). The median value for all subjects in that age group was ten affected surfaces.

The incidence of extracted permanent teeth was negligible among subjects who had not completed the shedding of their deciduous teeth. Among the subjects who were 14 to 19 years old, there was an average incidence of 0.5 extracted permanent teeth for each subject. When the incidence was considered in terms of the specific institution, it ranged from 0.0 to 0.73 (Table III). There was no correlation between the group incidence of extractions and the median incidence of caries.

The low incidence of filled cavities among the various groups is worthy of emphasis. The proportion of unfilled cavities to the total caries incidence ranged

TABLE I. NATURE AND SOURCE OF SUBJECT PERSONNEL

NO., AGE, AND DURATION OF RESIDENCE OF SUBJECTS	INSTITUTION NUMBER AND NATURE						TOTALS
	1 STATE ORPHANAGE	2 STATE SCHOOL*	3 CHURCH ORPHANAGE	4 STATE ORPHANAGE	5 CHURCH ORPHANAGE	6 STATE SCHOOL†	
Number of subjects:							
Boys	56	90	17	73	19	124	379
Girls	41	0	12	58	11	118	240
Total	97	90	29	131	30	242	619
Age range of subjects:							
Total range	10-19	10-19	6-14	11-19	8-14	6-19	6-19
Median value	14	16.5	9	13	11	14	14
Middle half of range	13-16	15-17	8-12	12-15	9-12	11-16	12-16
Duration of residence in institution (years):							
A. Those 6 to 13 years old:							
Median	3		3	4	2	3	
Mode	2		3	9	2	2	
B. Those 14 to 19 years old:							
Median	3	2		6		5	
Mode	2	2		9		9	
C. All subjects:							
Total range	-1 to 7	-1 to 7	-1 to 6	-1 to 9+	-1 to 9+	- 1 to 9+	-1 to 9+
Median value	2	2	3	5	2	4	3
Middle half of range	1-4	2-3	2-4	3-7	2-3	2-7.	2-6

*Industrial school for boys.
†School for the feeble-minded.

TABLE II. INCIDENCE OF CARIES OF PERMANENT TEETH IN TERMS OF AGE OF SUBJECTS

AGE	6	7	8	9	10	11	12	13	14	15	16	17	18	19	TOTAL
Number of subjects:															
Boys	4	7	9	12	16	20	48	38	50	53	43	40	26	13	379
Girls	4	6	13	8	12	15	24	30	27	27	25	21	19	9	240
Total	8	13	22	20	28	35	72	68	77	80	68	61	45	22	619
Number of subjects with no caries	5	5	1	0	0	0	5	3	3	0	1	1	1	1	25
Number of DMF* surfaces in permanent teeth:															
Median	*0.5*	*1*	*3*	*4*	*6*	*4*	*7*	*5*	*9*	*9*	*10*	*11*	*12*	*14*	
Range of middle half of values	0-4	0-5	2-6	4-5	5-8	2-7	3-9	5-9	5-14	5-14	6-15	7-20	8-17	8-24	
Total range of values	0-7	0-7	0-9	1-11	1-23	1-19	0-18	0-32	0-49	1-32	0-31	0-47	0-32	2-30	
Number of extracted permanent teeth	0	0	0	0	0	0	1	5	13	15	19	13	21	21	106

*DMF implies decayed, missing or filled; each extracted tooth is assumed to have had three carious surfaces.

TABLE III. INCIDENCE OF CARIES OF PERMANENT TEETH IN TERMS OF PLACE OF RESIDENCE

	INSTITUTION NUMBER						
	1	2	3	4	5	6	TOTALS
A. Subjects 6 to 9 years old, inclusive:							
Number subjects	0	0	16	0	10	37	63
Median age, months			93		107	97	97
Subjects with no caries			5		0	6	11
Number DMF* surfaces:							
Median value			*2*		*6*	*4*	*4*
Middle half of range			1-3		2-7	1-6	1-5
Total range of values			0-6		1-10	0-9	0-10
Extracted permanent teeth			0		0	2	2
Average number per child			0		0	0.06	0.03
Untreated caries (per cent unfilled)			79		96	100	96
B. Subjects 10 to 13 years, inclusive:							
Number subjects	37	3	9	61	17	74	201
Median age, months	152	138	145	148	143	147	
Subjects with no caries	3	1	0	8	0	0	12
Number DMF* surfaces							
Median value	*6*	*2*	*6.5*	*7*	*11*	*6*	*6*
Middle half of range	2-7		2-9	4-9	7-16	4-8	3-9
Total range of values	0-32	0-9	1-10	0-24	4-11	1-18	0-32
Extracted permanent teeth	5	0	0	0	0	10	15
Average number per child	0.135	0	0	0	0	0.135	0.075
Untreated caries (per cent unfilled)	56	100	57	47	92	95	73
C. Subjects 14 to 19 years, inclusive:							
Number subjects	60	88	3	69	4	131	355
Median age	180	199	172	181	167	194	
Subjects with no caries	1	1	0	0	0	4	6
Number DMF* surfaces							
Median value	*10*	*14*	*9*	*11*	*13*	*8*	*10*
Middle half of range	5-17	7-20		6-14		5-13	6-15
Total range of values	0-32	0-31	5-16	0-28	9-16	0-25	0-32
Extracted permanent teeth	40	64	0	8	2	66	180
Average number per child	0.67	0.73	0	0.12	0.04	0.50	0.50
Untreated caries (per cent unfilled)	47	85	60	41	80	91	73

*DMF implies decayed, missing or filled; each extracted tooth is assumed to have had three carious surfaces.

TABLE IV. CARIES INCIDENCE IN TERMS OF SEX FOR SUBJECTS AGED 14 TO 19 YEARS IN THREE CONTRASTED INSTITUTIONS

	NO. SUBJECTS	DMF* SURFACES		NO. EXTRACTED TEETH	NO. SUBJECTS WITH NO CARIES	MEDIAN AGE OF SUBJECTS (MO.)
		MEDIAN VALUE	MIDDLE HALF OF RANGE			
Institution 1						
Boys	29	*11*	5-21	14	1	181
Girls	31	*10*	7-16	26	0	180
Institution 4						
Boys	41	*10*	6-14	4	0	177
Girls	28	*11*	7-14	4	0	191
Institution 6						
Boys	67	*8*	4-13	35	2	193
Girls	64	*9*	5-13	31	2	195

*DMF implies decayed, missing or filled; each extracted tooth is considered to have had three carious surfaces.

TABLE V. INCIDENCE OF CARIES OF PERMANENT TEETH IN TERMS OF DURATION OF RESIDENCE IN INSTITUTION, FOR SUBJECTS 12 TO 19 YEARS OLD

	DURATION OF RESIDENCE								
	LESS THAN 4 YEARS			4 TO 7 YEARS			LONGER THAN 7 YEARS		
		DMF* SURFACES			DMF* SURFACES			DMF* SURFACES	
AGE	NO.	MEDIAN VALUE	MIDDLE HALF OF RANGE	NO.	MEDIAN VALUE	MIDDLE HALF OF RANGE	NO.	MEDIAN VALUE	MIDDLE HALF OF RANGE
12	33	*6*	4- 9	17	*6*	3- 9	17	*6*	3- 9
13	33	*7*	3- 8	22	*7.5*	5-10	18	*7*	4-11
14	31	*10*	3-14	33	*8*	6-12	12	*10*	4-15
15	34	*13*	6-17	21	*13*	5-18	26	*11*	5-14
16	28	*11*	7-17	13	*11.5*	7-13	13	*9*	6-11
17	29	*12*	7-24	14	*10.5*	8-18	14	*10.5*	5-20
18	18	*13*	9-23	9	*12*	11-19	12	*11.5*	6-15
19	9	*22*	15-18	5	*12*		7	*11*	

Averages for All 14 to 19 Years Old in Terms of Duration of Residence

LESS THAN 4 YEARS				4 TO 7 YEARS				LONGER THAN 7 YEARS			
NUMBER	AVERAGE AGE	NO. DMF* SURFACES	STANDARD DEVIATION	NUMBER	AVERAGE AGE	NO. DMF* SURFACES	STANDARD DEVIATION	NUMBER	AVERAGE AGE	NO. DMF* SURFACES	STANDARD DEVIATION
149	16.4	*13.6*	8.6	95	15.8	*11.6*	8.35	84	16.1	*10.6*	6.8

*DMF implies decayed, missing or filled; each extracted tooth is considered to have had three carious surfaces.

from 41 to 100 per cent in different institutions; for all subjects the average was 73 per cent. In other words, relatively few subjects had received reparative dental care.

The degree of personal attention to the teeth also was variable both for the individual and for the institution. At the time of each dental examination, the dentist scored the hygienic status of the mouth, designating it as satisfactory or unsatisfactory. Satisfactory implied that the teeth were reasonably clean and the gingival tissues were healthy; unsatisfactory connoted evidence of long-continued neglect and poor hygiene. The summated appraisal values for each of the six institutions indicated that unsatisfactory mouths prevailed at a 7 per cent level in the best rated institution, and at a 40 per cent level in the poorest. For institutions 1 to 6, the respective incidence of unsatisfactory oral hygiene was 11, 18, 7, 25, 10 and 40 per cent. These values showed no parallelism with the corresponding levels of caries (Table VI).

TABLE VI. INCIDENCE OF CARIES OF PERMANENT TEETH AS RELATED TO THE PERCENTILE INCIDENCE OF POOR MOUTH HYGIENE

INSTITUTION NUMBER	1	2	3	4	5	6
Median number of DMF* tooth surfaces:						
6 to 9 years old			2		6	4
10 to 13 years old	6		6½	7	11	6
14 to 19 years old	10	14	9	11	13	8
Percentile incidence of prolonged poor mouth hygiene	11	18	7	25	10	40

*DMF implies decayed, missing or filled; each extracted tooth is considered to have had three carious surfaces.

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Summarizing and comparing these various indices relating to caries, it will be noted that the institution with the lowest median carious incidence in the 14- to 19-year-old group (number 6) was also the most populous, and that its subjects had the highest relative incidence of unfilled cavities and of poorly kept mouths: the incidence of extracted teeth stood at the median level for all subjects of that age group. In contrast, the institution with the highest median caries score (number 2) stood highest as to the relative incidence of extractions, was second in number of subjects, about median as to oral hygiene, and next to the highest as to incidence of unfilled cavities.

One might question the validity of comparing dental findings among two populations, one of which was limited to boys while the other included both sexes. We observed no notable or consistent difference as to the extent of caries between the two sexes, and because of the commonness of caries experience it has been deemed justifiable to use pooled data for both sexes in our analyses. Table IV provides a comparison of caries incidence among boys and girls in the three institutions which housed both sexes and where the number of subjects was sufficient to give validity to the comparison. Although the table lists only subjects 14 years old or older, *sex variance was not evident* in any group living under the same conditions.

A reasonable explanation for the difference in caries incidence between the subjects from institutions 2 and 6 becomes apparent when one observes the correlation between the duration of residence under custodial conditions and the median caries scores. This is shown in Table V. Only those individuals who were 12 years old or older have been considered in this table. Duration of residence has been divided into three categories: less than four years, four to seven years, and longer than seven years. Summating all of the values for those 14 to 19 years old, the average number of DMF surfaces for each of the three mentioned groups was 13.6, 11.6, and 10.6, respectively. This downward trend of the means makes it obvious that *caries incidence has been lessened through prolonged institutional residence.* The difference between the means for those with the shortest and the longest period of residence is highly significant.

As a corollary of the caries incidence in terms of age, we have calculated the *average annual increment of caries progression.* Calculation was based on the premise that eruption of the permanent teeth had begun at the age of 6 years. For any group of children the rate could be obtained by dividing the total number of affected tooth surfaces by the pooled values (for age in years minus six) for each child included in the group. Values were calculated for all subjects aged 8 to 12, 13 to 15, and 16 to 19 years old, inclusive. The resultant figures are shown in Table VII, together with a separate consideration within each group for those who had been in residence for six years or longer, and further for those in residence at least nine years. The values ranged from a high of 1.3 to a low of 0.7 newly carious surfaces per annum; those with the longest period of residence had the lowest increment value. This illustrates again the trend for caries progression to decelerate with prolonged institution life.

Lactobacillus acidophilus studies of saliva were made as a part of the dental examinations of the children in institutions 2, 3, 4, and 5. The results of these

TABLE VII. CALCULATED CARIES INCREMENT RATE: AVERAGE NUMBER OF NEWLY CARIOUS TOOTH SURFACES PER ANNUM FOR EACH SUBJECT

AGE AT TIME OF EXAMINATION	AVERAGE ANNUAL INCREMENT RATE		
	ALL SUBJECTS	THOSE IN RESIDENCE 6 YEARS OR LONGER	THOSE IN RESIDENCE 9 YEARS OR LONGER
8 to 12 years	1.3	1.1	1.2
13 to 15 years	1.3	1.3	1.1
16 to 19 years	1.2	1.0	0.7

studies have been included in the earlier report.[3] Recently we have re-examined the mouths of the children from institution 6, and included *L. acidophilus* estimation as a part of the routine. These studies will be reported at a later time. In general, it may be said that the counts of *L. acidophilus* have ranged widely, with no apparent correlation between the number of organisms and the past or current state of caries advance.

The fluorine content of the domestic water supplies used by the six institutions has been determined frequently, using currently accepted methods of analysis.[4] The water from institution 6 contained 0.4 part of fluorine per million. Samples from the other institutions contained not more than a trace at any time. There is no evidence that the caries progress of the subjects could have been affected significantly through the ingestion of fluorine during the periods of custodial care. It is less easy, however, to determine whether significant amounts of fluorine may have been ingested by some of the subjects prior to the time of commitment. Water analyses made a decade ago offered the impression that significant amounts of fluorine could be found in certain wells in practically every county of the state, even though water from other wells in the same community was reported fluorine free. More recent analyses made with the currently standard techniques have shown lesser amounts of fluorine from specific sources, suggesting that the earlier values may be accepted only with caution. Fluorosis, however, is endemic in certain sections of the state. In such areas the incidence of mottled enamel is high. However, one cannot properly assume that all enamel areas presenting pitting of the yellowish-white or brownish type are evidences of fluorosis wherever they may be found; neither can the role of fluorine in the production of such areas be dismissed without proof. If one were to attribute all lesions of the type just described to fluorine ingestion during the period of enamel deposition, then, from the clinical incidence of such a hypoplastic condition, he would be forced to assume that approximately one-third of the pooled subjects from institutions 1 to 5 inclusive, and about 40 per cent of those from institution 6 had received significant amounts of fluorine for considerable periods of time prior to reaching the age of 6 years. As has been previously reported,[3] there was less caries among the subjects with so-called mottled enamel from institutions 1, 2 and 4 than among those with no mottling from the same institutions: the difference approached a significant level. Among the subjects from institution 6, on the other hand, there was no consistent or significant difference as to the mean caries incidence for those with or without so-called mottling of the enamel (Table VIII). Even though the possible protective effect from early fluorine ingestion cannot be disproved from the data

at hand, there is no reason to attribute distinctive significance to fluorine effect among the children included in these studies. If it were true that initial caries resistance was due to fluorine ingestion, one would expect a low caries incidence among the younger subjects and those who had recently come from areas of possible fluorine supply. The data indicate, on the contrary, that these differences were not apparent, but rather that the longer the subjects remained in the institutions, the less rapidly their caries tended to progress.

TABLE VIII. INCIDENCE OF CARIES OF PERMANENT TEETH AS RELATED TO PRESENCE OR ABSENCE OF HYPOPLASTIC ("MOTTLED") ENAMEL

AGE	1. WITH ENAMEL HYPOPLASIA			2. WITHOUT ENAMEL HYPOPLASIA			DIFFERENCE OF MEANS (2-1)	STANDARD ERROR OF DIFFERENCE	RATIO DIFF./STANDARD ERROR OF DIFFERENCE
	NO. SUBJECTS	DMF* SURFACES MEAN	DMF* SURFACES STANDARD DEVIATION	NO. SUBJECTS	DMF* SURFACES MEAN	DMF* SURFACES STANDARD DEVIATION			
Children from Institution 6									
6 to 9 years	13	*3.9*	3.3	21	*3.6*	2.3	−0.3	1.0	0.33
10 to 13 years	34	*7.15*	3.6	37	*5.3*	4.1	−1.35	0.9	1.5
14 to 19 years	47	*10.2*	9.1	72	*11.2*	7.0	+1.0	1.47	0.68
Children from Institutions 1 to 5 Inclusive†									
14 to 19 years	77	*11.1*	7.8	146	*14.0*	9.25	+2.9	1.17	2.48

*DMF implies decayed, missing or filled; each extracted tooth is considered to have had three carious surfaces.

†Data taken from previous publication.[3]

DISCUSSION

These epidemiologic studies of caries are based on comparisons between certain indices relating to tooth decay in contrasted child populations. For such comparisons to have validity, it is necessary that the data be collected under similar conditions. Other studies regarding the constancy of dental findings have demonstrated that widely different values may be obtained by successive observers for the same population, or even for the same mouth.[5] To eliminate the human equation as much as possible, it is best that all examinations subject to comparison be made by the same individual under rigid standard conditions. If more than one examiner must be used, every effort should be made to assure similarity of appraisal and of methodology. The ideal dental examination should be unhurried. It should provide for initial operative cleansing of the teeth, and the drying of each exposed tooth surface prior to its detailed examination by means of sharp explorers and mouth mirror with adequate illumination. Accounting should be made for each tooth space. The clinical findings should be verified or extended by means of complete dental roentgenograms. The record should indicate the site, extent, and present activity or softness of each dental lesion, compiled with a statement as to evidences of earlier treatment. Also, there should be included statements concerning the status and apparent health of the supporting tissues, taking into account the degree of cleanliness and evident care of the mouth.

The current study approximated the stated ideals as well as circumstances would permit. It was not possible to clean the teeth as a preliminary measure,

nor were the surfaces always dried prior to examination. The dental examinations in institutions 1 to 5 inclusive were all made by the same examiner, after he had been especially trained in the desired technique. Several examiners participated in the study at institution 6, but the work was well supervised and the individual examiners had been adequately trained. Roentgenograms were made part of the examination only in institution 6. The x-ray examination revealed an additional 6 per cent of presumably carious lesions, 70 per cent of which were confined to the enamel and minor in extent. On the basis of this ratio, it is unlikely that roentgen examination of the mouths of subjects from the other institutions would have changed the carious scores in significant degree.

Our interpretations would be enhanced if, as a basis for comparison, we had data relating to a typical Iowa public school population, collected by our own examiners using the techniques employed for the institution subjects. Such values are not now available. The values for the dental clinic clientele, reported in the first of this series,[1] are not comparable because they represent children coming specifically for dental services. Moreover, they represent preponderantly a different age group. The study of the dental clinic clientele was designed particularly to show the long-term caries course in individual subjects who were living under nonregimented conditions.

It is reasonable to believe that the data for caries incidence among the school population of Hagerstown provide a fair measure of the average caries extent one might expect to find in a typical school population where no specific regimentation of living conditions has prevailed.[2] The techniques of examination described in the reports of the Hagerstown studies apparently correspond closely with those employed in the current study. Table IX presents a comparison of the average findings for several items from the total institution population and from the Hagerstown group. To obtain similar values for comparison, it has been necessary to recalculate the published Hagerstown values so as to combine those for boys and for girls, and also for overlapping age groups in the elementary and high school populations. Moreover, in view of the fact that in the Hagerstown data a value of five affected surfaces has been assigned for each extracted tooth, in contrast to our allowance of but three, we have calculated those data in terms of each coefficient and listed both values.

It will be noted that initially the institution subjects tended to have more caries than did the public school controls; but during the postshedding years this trend was reversed. Instead of showing progressive acceleration of the rate of caries as did the Hagerstown subjects, the rate tended to decelerate among those who had spent considerable intervals under custodial care. This difference will be further emphasized if reference is made to the values given in Table VI for the postshedding groups with different duration of residence.

Undoubtedly, the difference between the contrasted child populations are greater than the data indicate. The DMF scores exaggerated the amount of tooth destruction actually present among these institution subjects, because the cavities as a whole were minimal in extent, frequently limited to pits and

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TABLE IX. INCIDENCE OF CARIES OF PERMANENT TEETH FOR INSTITUTION SUBJECTS COMPARED WITH VALUES FROM THE HAGERSTOWN PUBLIC SCHOOL POPULATION

AGE	6	7	8	9	10	11	12	13	14	15	16	17	18	19
DMF* surfaces for each child; mean:														
Institution subjects (with $M = 3$)*	1.9	2.5	3.9	4.8	6.8	5.4	6.6	7.4	10.5	11.0	10.7	13.0	13.4	15.4
Hagerstown subjects (with $M = 3$)*	0.4	1.0	1.6	3.5	4.4	4.7	8.1	7.5	9.6	11.5	12.7	13.9	16.3	19.0
(with $M = 5$)	0.6	1.0	1.7	3.8	4.9	5.2	7.2	8.9	10.9	13.3	14.7	16.4	19.8	24.6
Average number of extracted permanent teeth per capita:														
Institution subjects		0.03				0.075					0.5			
Hagerstown subjects		0.057				0.35					1.0			
Incidence of untreated caries (per cent of cavities unfilled):														
Institution subjects		96				73					73			
Hagerstown subjects		62				47					30			

*DMF implies decayed, missing or filled; each extracted tooth is considered to have had three or five carious surfaces prior to extraction, as indicated in the table.

fissures, and with no apparent dentinal involvement. Nevertheless, such areas were included among the score of affected surfaces if there was any question as to the presence of enamel caries. Moreover, the exposed dentin in many open cavities was flintlike in consistency, giving the impression that caries had become arrested. The incidence of extracted teeth was low, and some extractions obviously had been made not because of caries but because of periodontal disease in mouths where little or no caries was evident. Other teeth evidently had been extracted as a simple means of relieving the patient's discomfort, without an attempt to conserve the tooth. The general status of the whole population, therefore, made it more justifiable to score extracted teeth on the assumption that an average of three rather than five surfaces had been affected by decay. If our interests in this study were directed toward tooth mortality rather than toward caries, we would consider that the extraction of a posterior tooth necessarily led to the loss of five exposed surfaces. Since instead we are concerned primarily with the measurement of the extent of decay, it seems inexact to employ any arbitrary coefficient as a measure of the pre-extractive extent of caries in a given tooth; instead, it would be better in each instance to base the estimate on the collateral extent of decay in the remaining teeth. To avoid individualization we have accepted an average of three affected surfaces for each extracted tooth; with consideration of the general dental status of the entire population included in our survey, this seems to be a conservative estimate. Work now in progress tends to substantiate this concept.[6]

One may assume that the general status of the mouths of the Hagerstown children led the investigators to assign the value of five affected surfaces to each extracted tooth among those children. If such an assumption be correct, then it is proper to compare the present data, based on a coefficient of three affected surfaces, with the Hagerstown data in which the coefficient is five. The validity of such an assumption is open to question. When corresponding coefficients are employed for the two contrasted groups, the most striking differences be-

tween the two sets of values are the initially greater incidence among the institution subjects, and the reverse situation among those in the middle and late teen years. It is among these older subjects that the ones with the longest periods of institutional residence are included, so it seems reasonable to attribute their lessened caries scores to some factor associated with their institution life.

The Hagerstown children as a group offered evidence of more professional dental care than did the institution populations. The nature and amount of such care in our subjects differed, however, from one institution to another. For example, in institution 4 the children received frequent and excellent medical and dental supervision. Hygienic dental measures were employed routinely and major cavities were filled promptly. The children were trained to brush their teeth regularly and thoroughly, and facilities were provided for the purpose. In institutions 1 and 2 conditions were somewhat similar, but dental services were more limited. In institution 6, facilities for dental care were inconstant and inadequate. We have no data for the entire population from institution 6 because in our survey only those subjects were included who were able to cooperate sufficiently to permit the performance of an adequate dental examination. Of the subjects examined, few had received professional dental care other than the removal of offending teeth. The routine of tooth-brushing was practiced among these children, but with widely variable efficacy due to the limited capacity of the subjects to participate actively.

From the preponderance of unfilled cavities among the total institution population, one must conclude that the lack of dental treatment had not of itself led to the noteworthy furtherance of caries. In fact, this lack of dental care may tend to lessen the apparent incidence of decay. This paradox is understandable if one realizes that any filling of necessity must be larger than the area of caries it is designed to replace. Furthermore, in child populations where pits and fissures of the enamel are filled routinely as a prophylactic measure designed to prevent the development of decay in such regions, one cannot know whether such areas would have become carious if the prophylactic fillings had not been placed. Contrary to prevailing dental philosophy[7] one need not assume that all deep pits or fissures will lead to caries. In populations where conditions tend to retard caries, such supposedly susceptible areas may remain noncarious until they have become obliterated through attritional wear.

Even though lack of dental care has not led to notable caries advance among these subjects, lack of recurrent dental care is not to be condoned. Both the studies of the Hagerstown children[2] and of our dental clinic clientele[1] make it evident that whereas professional dental care does not prevent the development of new carious lesions, it does serve to check its local advance and lessen tooth mortality.

Among the Hagerstown subjects the girls had a higher incidence of caries in terms of age than did the boys. This was attributed to the fact that girls tend to erupt their permanent teeth at an earlier age than do boys, and as a consequence, at any given age the teeth of girls have been exposed to caries-producing influences for a longer interval of time. In the clientele of the dental

clinic[1] we observed a similarly greater incidence of caries among girls than boys, but when studied in terms of posteruptive age of specific teeth, we could not relate the difference to the posteruptive age of the teeth. Instead we attributed the sex difference to the poorer habits of eating encountered in girls. This institution study permits further exploration of sex differences in caries incidence. Among these children who were living under conditions of regimentation, no sex difference in caries experience could be established. Under institutional conditions of living the boys and girls ate the same types of food, and the children were given less opportunity to choose or to reject than is common in the average home. One may properly infer from this lack of sex difference that when such differences are encountered they are due to living practices rather than to sex per se or to posteruptive tooth age. One may assume that if conditions of life are such that the trend toward caries is depressed, time will cease to be the most significant factor governing the extent of caries in the individual mouth.

Of the 14- to 19-year-old subjects living in the more populous institutions, only the boys from the industrial school (institution 2) had a median DMF value which exceeded the mean value for the corresponding Hagerstown population. One would predict this difference, if factors relating directly to custodial care were primarily concerned with the lessening of caries progress. The commonest term of residence in the industrial school was one and one-half to two years. Moreover, the average age at the time of commitment was 15½ years. The socioeconomic status of these boys prior to commitment had not been favorable. In greatest number they represent dependent, neglected, or delinquent boys, most of whom came from broken homes. Therefore, one may assume that the caries found in their teeth reflected primarily their precommitment status.

In contrast to the industrial school population, most of the inmates of institution 4 were committed during infancy. Records for that orphanage indicate that some infants are adopted soon after entering the institution, but that most of the others may be expected to remain state charges until they reach young adulthood. Often, however, such children will spend periods of months or longer in private homes, then ultimately be returned to the institution. The situation in institution 1 is similar, except that inmates are not accepted there until they are 6 years of age or older. The age at commitment for the children at the school for the feeble-minded varies widely. With minor exception, the period of commitment extends throughout life.

Current medical philosophy calls for the consideration of emotional factors as they may affect organic disease. Until there is evidence to the contrary, one cannot properly assume that prolonged emotional tension may not favor the development of caries. We have not studied specifically such interrelationship, but recognize this need for its further investigation. Under favorable conditions, one may expect lessening of certain tensions among children under custodial care. Such children have less stimulating environments than do children living in private homes, and likewise they have less personal responsibility than does the child who must carry his own initiative at home and at school. Though it

is recognized that the atmosphere even in a well-managed custodial institution fails to personalize a child and tends to dwarf his capacity for self-expression, yet it avoids some of the emotional tensions which characterize home life; it is noncompetitive and predictable. Emotional tension and a sense of personal insecurity were present among the boys in the industrial school; these traits were least notable among the children in the institution for the feeble-minded. The mentally retarded child usually accepts the environment and protection offered by a good institution, and frequently is much happier there than he would be living in the average private home where he would be brought into competition with his more capable associates.

An attempt was made to determine the characteristics of the diet in the four state-controlled institutions.[8] A worker specially trained in dietetics visited each institution, where she observed eating practices, collected menus employed during considerable periods of time, studied the over-all consumption of key foodstuffs from records of purchase and production, and calculated the apparent adequacy of intake of specific nutrients. Some aspects of that study have proved contradictory, and others are difficult to interpret. It was not uniformly possible to distinguish between foods eaten by inmates and those eaten exclusively by the employed personnel. One cannot make sure that conditions as they were observed were typical of those which prevailed at other times. Certain conclusions, however, may be deduced. There was little variation from child to child in a respective institution as to the type of food each received. Children were trained and expected to eat the food served without waste. Each child ate three meals daily. Milk was supplied in fair abundance; in some instances it even comprised a disproportionate amount of the protein supply. Vegetables and fruits probably were offered in adequate amount, even though the variety might be slight. No child was deprived of an ample supply of calorific foods. A high proportion of the calories was derived from carbohydrate sources. Sugar consumption during the prerationing days had not been restricted. From an analysis of the total amount consumed semiannually, it was estimated that the daily per capita consumption ranged from 2 oz. in institution 2 to almost 4 oz. in the other institutions. One would not classify the diets as optimum, yet, because of their constancy and their universal consumption alone they probably were superior to those eaten by many Iowa children living in private homes.[9] Because of the findings in earlier reported studies[10] the authors are inclined to attribute the lessened caries experience among these regimented children principally to factors associated with their intake and utilization of food.

As a gross means of appraising the over-all nutritional status, the height and weight of each child were measured at the time of the dental examination. The measurements have been compared with standards for Iowa children from middle-class homes.[11] The observed values were classified in relation to the degree in which each deviated above or below the standard median or mean. It then was possible to compare the degree of deviation for weight in terms of age with the corresponding deviation of height for age. Using this procedure it was found that in institutions 1 and 2 the weight tended to be about one standard deviation greater than would have been predicted from the corresponding height.

This may reflect the liberal ingestion of preponderantly carbohydrate foods. In the remaining institutions the median weight and height relationships tended to be in close agreement.

SUMMARY AND CONCLUSIONS

The incidence and extent of dental caries have been measured in 619 children resident in six custodial institutions. The caries scores of individual subjects and the average scores for respective institutions have been compared, and contrasted with corresponding values reported for a general public school population at successive age levels.

Among the younger children, the institution subjects had a higher average incidence of caries than did the corresponding public school population, but during the postshedding period the average caries incidence was significantly less among the children who had lived for several years under institutional regimentation. Those who had lived longest under custodial care had the lowest median incidence of caries. No sex difference in caries extent was evident. There was no relationship between the amount of prophylactic or therapeutic dental care the children had received and their respective caries scores. The majority of the children examined had been given meager dental care, and many showed evidence of prolonged neglect of oral hygiene.

The data presented in this report support the thesis that regimentation of living conditions may of itself modify caries experience, without evident relation to intraoral environmental factors. The mechanisms which have led to reduction of caries among these children have not yet been established. However, there is no evidence that the benefit can be attributed to the ingestion of fluorine, to reparative dental services, or to oral hygiene. These children received diets high in total carbohydrate content, and prior to the recent emergency the individual consumption of sugar had been high.

It seems probable that the lessening of caries in these children may properly be attributed to the constancy of environmental patterns, the freedom from certain emotional stresses, the regularity and constancy of food intake, and the regular inclusion in the diet of certain protective foods. Analysis of the diets employed in these institutions reveals that, though they did not meet all the standards for optimum nutrition, they were better and more constantly dependable in certain regards than those ingested by the average child.

This study is one of a series of reports dealing with the dental findings among specific groups of children, each living under such environmental conditions that certain of the variables encountered in the general child population can be eliminated from consideration. The complete series is planned ultimately to offer evidence as to the role various factors may play in the epidemiology of dental caries.

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REFERENCES

1. Boyd, J. D., and Cheyne, V. D.: Epidemiologic Studies in Dental Caries: I. The Pattern of Dental Caries in Iowa City Children, J. PEDIAT. **29**: 157, 1946.
2. Klein, H., Palmer, C. E., and Knutson, J. W.: Dental Status and Dental Needs of Elementary School Children. Pub. Health Rep. **53**: 751, 1938.
   Klein, H., and Palmer, C. E.: The Prevalence and Incidence of Dental Caries Experience, Dental Care and Carious Defects Requiring Treatment in High School Children, Pub. Health Rep. **55**: 1258, 1940.
3. Boyd, J. D., and Cheyne, V. D.: To What Extent Does Fluorine Ingestion Lessen Tooth Decay? J. PEDIAT. **29**: 286, 1946.
4. Iowa State Planning Board: Mineral Analyses of the Underground Waters of Iowa, State Printing Board, 1938; also additional unpublished analyses from the State Water Laboratories.
5. Deatherage, C. F., Wilson, L. A., and Ledgewood, R.: Variability of Routine Diagnoses of Dental Defects in Children of School Age. J. Am. Dent. A. **26**: 1739, 1939.
   Radusch, D. F.: Variability of Diagnoses of Incidence of Dental Caries, J. Am. Dent. A. **28**: 1959, 1941.
6. Wessels, K. E., and Cheyne, V. D.: Unpublished data.
7. Hyatt, T. P.: Dental Cosmos **65**: 234, 1923.
8. Boyd, J. D., and Scott, Louise A.: Unpublished data.
9. Boyd, J. D.: The Need for Betterment of Children's Diets, J. Am. Dietet. A. **20**: 147, 1944.
   Idem: Prescribed Diets for Normal Children, J. PEDIAT. **24**: 616, 1944.
10. Boyd, J. D.: Prevention of Dental Caries in Late Childhood and Adolescence, J. Am. Dent. A. **30**: 670, 1943; Dietary Control of Enamel Caries, Ibid. **30**: 1344, 1943.
    Idem: Long-Term Prevention of Dental Caries Among Diabetic Children, Am. J. Dis. Child. **66**: 349, 1943.
11. Jackson, R. L., and Kelly, H. G.: Growth Charts for Use in Pediatric Practice, J. PEDIAT. **27**: 215, 1945.

SYDENHAM'S CHOREA, A SYNDROME FOR DIFFERENTIAL DIAGNOSIS

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CURRENT pediatric texts consider Sydenham's chorea to be a manifestation of rheumatic fever.[1-3] In active rheumatic fever, an increased erythrocyte sedimentation rate (ESR) is an almost constant finding, except in the presence of cardiac decompensation and in some cases of chorea. This study was planned to consider the differences, if any, between those patients with chorea having an increased erythrocyte sedimentation rate, and those patients with chorea having a normal erythrocyte sedimentation rate.

MATERIAL AND METHOD

The patients studied were all those admitted to the Michael Reese Hospital between 1934 and 1947 who had chorea and upon whom erythrocyte sedimentation rates were done. Of the total of 107 patients, eighty-eight were seen during their first episode of chorea and followed thereafter, and nineteen were seen for the first time during their second or a subsequent episode of chorea and followed thereafter. (Charts 1 and 2. One case is not listed on the charts, but is discussed below.) Erythrocyte sedimentation rates were done by the Landau technique[4] (normal established by Herzog[5]). A thorough follow-up study was made.

DATA

The patients were grouped in the following manner:

Group I. Patients studied during initial episodes of chorea
- a. with an increased ESR
- b. with a normal ESR

Group II. Subsequent episodes of chorea in patients of Group I
- a. from Group I, a.
- b. from Group I, b.

Group III. Patients not seen during first episode of chorea, but seen for the first time during subsequent choreic episodes.

Group I, a.—Patients Seen During Initial Episode of Chorea with Increased Erythrocyte Sedimentation Rate.—Of the eighty-eight patients seen during their first episode of chorea, thirty-seven (42 per cent) had erythrocyte sedimentation rates which were above normal. Of these thirty-seven, nineteen (51 per cent) had active rheumatic heart disease at the time of admission. Twelve of the remainder showed other evidences of active rheumatic fever (muscle pains, fever, arthritis, etc.) either immediately preceding or concurrent with

From the Kunstadter Laboratories for Pediatric Research and Sarah Morris Hospital of Michael Reese.

the chorea; six showed no other evidence suggestive of rheumatic fever except the increased sedimentation rate. Thus, of thirty-seven patients experiencing a first episode of chorea accompanied by an increased erythrocyte sedimentation rate, thirty-one (84 per cent) showed other evidence of rheumatic activity at that time.

Of the eighteen patients who did not have heart involvement during the first episode of chorea, four developed it subsequently. All four were from among those twelve patients who had had other rheumatic manifestations during the first episode of chorea. None of the six patients who had had no other suggestive evidence of rheumatic fever developed heart involvement subsequently. The latter six patients are discussed below. Thus, twenty-three of the thirty-seven patients (62 per cent) with chorea and an increased sedimentation rate eventually developed rheumatic heart disease. Of these thirty-seven patients, five were followed for six months, nine for from one to four years, and twelve for from four to twelve years.

Emotional disturbances, such as irritability, crying easily, talkativeness, and disobedience were noted in eleven (30 per cent) of these thirty-seven patients.

Group I, b.—Patients Seen During Initial Episode of Chorea with Normal Erythrocyte Sedimentation Rate.—Of the eighty-eight patients seen during their first episode of chorea, fifty-one (58 per cent) had normal erythrocyte sedimentation rates. Not one of these showed any other evidence of active rheumatic fever during these admissions; only one gave a history of rheumatic fever. (The latter is not shown on the chart, but is discussed below.) Fifteen were followed for five to eleven years thereafter, and fourteen for between one and five years, and none of these developed rheumatic fever subsequently at any time.

In this group, psychic factors far outweighed in number and character those noted in the cases of Group I, a. The more common of the obvious psychic disturbances in this group were irritability; crying easily; being temperamental, disobedient, stubborn, selfish, cross, impulsive; having temper tantrums, feelings of inferiority at school; stealing; loss of interest in school; excitability; and fearfulness. Such symptoms were noted in thirty-three of these fifty-one patients (65 per cent).

Two patients in this group developed their first episode of chorea following a severe fright, one following and accompanied by a profound emotional reaction set off by a change to a new and more stringent teacher, two following a first menstrual period for which they were mentally unprepared, and one occurring in an emotionally distraught girl whose most intimate playmate had just recovered from chorea. Such striking associations were not noted in any of the cases of chorea which had an increased erythrocyte sedimentation rate (Group I, a above).

Group II, a.—Subsequent Episodes of Chorea in Patients from Group I, a.—Of the thirty-seven patients who were seen during their first episode of chorea and who at that time had increased sedimentation rates, nine (24 per cent) had

one or more recurrences. As can be seen in Chart 1, three of these recurred from among the nineteen of the thirty-seven patients who had had during the initial episode other evidences of rheumatic activity and also active rheumatic heart disease. During this first recurrence among these three patients, two again had increased sedimentation rates, other evidences of rheumatic activity, and active rheumatic heart disease, and one of the two had a second recurrence with an increased erythrocyte sedimentation rate, other evidence of rheumatic activity, and active rheumatic heart disease. One of the three patients of this group of nineteen had a first recurrence with a normal sedimentation rate, inactive heart disease, and showed no other evidence of rheumatic activity. The latter recurrence is discussed further, below.

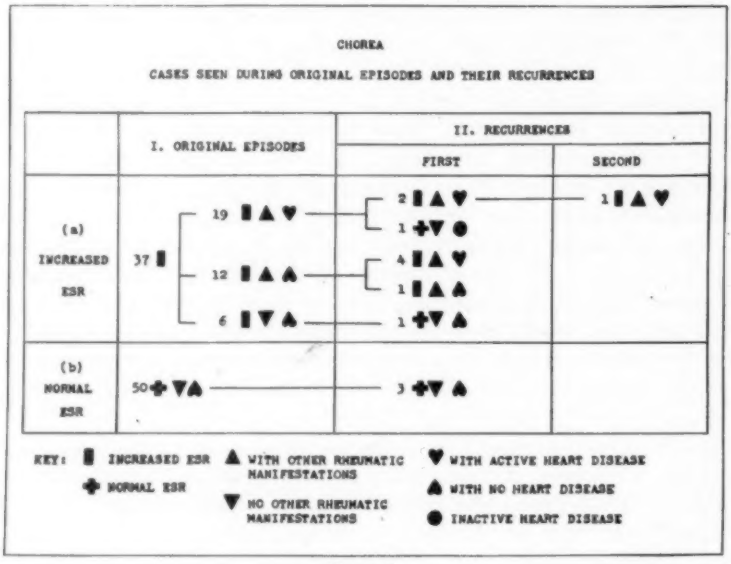

Chart 1.

Five of these recurrences were from among the twelve of the thirty-seven patients who, during their initial episode, had an increased erythrocyte sedimentation rate, other evidence of rheumatic activity, but no evidence of heart involvement. During their first recurrence, all five again had increased erythrocyte sedimentation rates and other evidences of rheumatic activity. In addition, four of these patients developed active rheumatic heart disease for the first time.

One of the recurrences was from among the six of the thirty-seven patients who, during their initial episodes, had increased sedimentation rates, no other evidence of rheumatic activity, and no heart involvement. However, this patient had a normal sedimentation rate during the first recurrence, and still had no evidence of heart involvement or rheumatic activity. It should be pointed out at this time that the sedimentation rates in the latter six patients, during

their initial episode, were only slightly above the accepted normal (range 20 to 30, average 22, as compared with the other thirty-one cases in this group of thirty-seven, range 20 to 55, average 29). This group is discussed further below.

Group II, b.—Subsequent Episodes of Chorea in Patients from Group I, b.—Of the fifty-one patients who were seen during their first episode of chorea and who at that time had normal sedimentation rates and no other evidence of rheumatic fever, three (6 per cent) had a recurrence. As can be seen in Chart 1, each of these three patients had one recurrence. Again the sedimentation rates were all normal, and there was no other evidence of rheumatic activity and no sign of heart disease.

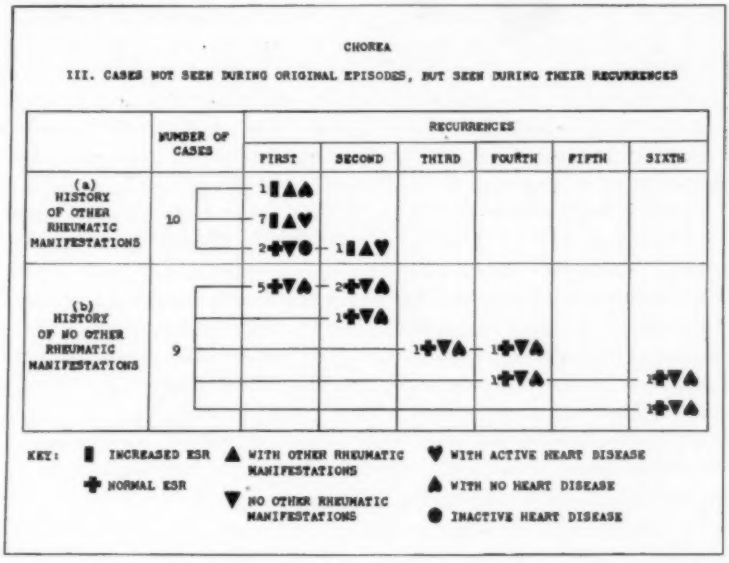

Chart 2.

Group III.—Patients Who Were Not Seen During Their Initial Episode of Chorea, but Who Were Seen for the First Time During Subsequent Episodes.—Of the total of 107 patients with chorea, nineteen were not seen during their first episode. Because of the above results, these nineteen patients were also divided into two subgroups: (a) those with a history of other rheumatic manifestations during their previous or first episodes of chorea, and (b) those with no other evidence of rheumatic activity in their previous history (see Chart 2).

Group III, a. Patients with a History of Other Rheumatic Manifestations During a Previous Episode of Chorea.—Of the nineteen patients who were not studied during their first episode of chorea ten gave a history of having had other signs of rheumatic activity. Of these ten patients, nine gave a history of active rheumatic heart disease as well as other signs of rheumatic activity during a previous episode, and one gave a history of other evidence of rheumatic activity but without heart involvement.

As can be seen in Chart II, eight of these ten patients had one recurrence during which each had an increased sedimentation rate as well as other evidence of rheumatic activity. Seven of these eight patients had, in addition to the other signs of activity, active rheumatic heart disease, and one still had no heart involvement.

Two of these ten patients who gave a history of other signs of rheumatic activity during their first episode of chorea had, during their first recurrence, normal sedimentation rates and evidence of inactive rheumatic heart disease. These recurrences are discussed below. Of these two patients, one had a second recurrence, this time with an increased erythrocyte sedimentation rate, other evidence of rheumatic activity, and active rheumatic heart disease.

Group III, b. Patients with History of Previous Episode of Chorea Without Other Evidence of Rheumatic Infection.—Of the nineteen patients who were not studied during their first episodes of chorea, nine gave no history of other rheumatic activity at any time. Again referring to Chart 2, it can be seen that these nine patients were seen for the first time during their first or during a subsequent recurrence. There was no history of any other evidence of rheumatic fever during the previous episodes of chorea in any of these cases. All had normal erythrocyte sedimentation rates and none showed other evidence of rheumatic activity or of heart involvement during these recurrences. Five patients were seen for the first time during their first recurrence, and of these, two had a second recurrence. One patient was seen for the first time during his second recurrence; another for the first time during his third recurrence (this child subsequently had a fourth recurrence); one was seen first during his fourth recurrence, not during his fifth recurrence but again during his sixth recurrence; and one was seen for the first time during his sixth recurrence. All had sedimentation rates which were normal, and none showed other evidence of rheumatic activity or heart involvement at any time.

Briefly, these nine patients gave a history of a total of twenty previous episodes of chorea with no other evidence of rheumatic activity. They had a total of thirteen recurrences which were studied. Each time the sedimentation rates were normal and none showed evidence of heart disease at any time nor any other sign of rheumatic activity.

ANALYSIS OF DATA

It is quite clear from the above that chorea associated with an increased erythrocyte sedimentation rate is in most instances a manifestation of active rheumatic fever. Eighty-four per cent of patients with chorea and an increased sedimentation rate showed other evidence of rheumatic activity, and 62 per cent of these eventually developed rheumatic heart disease. It is equally clear that patients who have a normal erythrocyte sedimentation rate during their first episode of chorea do not have rheumatic fever and are no more subject to its sequelae than are other members of the population.

In the cases of nonrheumatic chorea it was shown that psychogenic factors were far more numerous and varied than in the cases of rheumatic chorea.

The temporal relationship to the onset of the choreic episode and the striking nature of certain psychogenic factors emphasize the probable etiologic role of psychic disturbance in this form of chorea. Such dynamic inciting factors as severe fright, unanticipated onset of menses, and a markedly disturbing change of teachers immediately preceding these episodes are good examples. One patient who was emotionally distraught, developed nonrheumatic chorea just after an intimate playmate had recovered from chorea. This suggests that in some cases imitation may be a factor. The concept of psychogenic chorea is not new. Indeed, before the discovery that rheumatic fever was a common cause it was generally believed that most chorea was psychogenic.

Hughes,[6] who made a careful study of this syndrome, reported a case wherein sudden fright not only incited the chorea, but a second fright caused it to stop. "A girl, who had been in the hospital for chorea, and who went out cured, had a return of her complaint. She was going to the hospital to apply for readmission, but, on her way, was much alarmed as she passed over London Bridge by a person being run over. She, however, pursued her course. On her arrival at the room in which the patients are selected for admission, both she and her mother were much surprised to find that the complaint had left her. She, therefore, went home again, and had not, so far as I know, any return of this disorder."

Recurrences may occur both in patients with rheumatic chorea and in those with nonrheumatic chorea. Recurrences were more common in the patients with rheumatic chorea (24 per cent) than in those patients with nonrheumatic chorea (6 per cent). Recurrences among patients with nonrheumatic chorea were always nonrheumatic. However, it can be seen from the data above and from Charts 1 and 2 that among the forty-eight patients with rheumatic chorea, there were four recurrences during which there was no other evidence of rheumatic activity and during which the erythrocyte sedimentation rates were normal.

Three of these recurrences seemed to be precipitated by psychogenic factors similar to those noted in nonrheumatic chorea. The home environment of one patient was characterized by a constant change from one unhappy foster home to another. One recurrence developed in a patient who returned to a home where she was very much resented by her mother and siblings, and where the home situation was characterized by jail sentences for the father and lack of moral code in the rest of the family. One developed in a patient whose family was irrationally overanxious about the possibility of a recurrence of the previous episode of rheumatic chorea. Thus, chorea may recur in a patient who has previously had rheumatic chorea, and the recurrence may be associated with a normal erythrocyte sedimentation rate. However, as in the above patients, such recurrences may be on a psychogenic rather than on a rheumatic basis. This would explain the normal sedimentation rate and lack of other evidence of rheumatic activity during these recurrences. Analyzing the dynamics involved in the first two of the above patients, one may reason that they found chorea to be a means of escape from unhappy home situations to the relatively secure,

and for them, happier surroundings of the hospital. These recurrences, therefore, may be imitative, this time in imitation of a previous rheumatic chorea in the same patient. It is our concept that if chorea can be imitative, it is not so on a conscious level any more than are tics.

There remains for analysis the six patients (Group I a, Chart 1), who had chorea with an increased sedimentation rate and no other evidence of rheumatic fever. One of these had a recurrence with a normal sedimentation rate and no other evidence of rheumatic infection. Two of these patients had sedimentation rates of 25 and 30, but in four the sedimentation rates were only 2 mm. above the accepted upper limit of normal. It is quite possible therefore, that the basis for chorea in the latter four patients at least was also nonrheumatic, and that the cause of the slightly elevated sedimentation rates was something other than rheumatic fever. There is insufficient data to evaluate these particular cases as either rheumatic, psychogenic, or of other cause.

RE-EVALUATION OF THE LITERATURE

The evidence for the concept of a rheumatic and a nonrheumatic chorea given above is so clear and of such great importance that it was considered necessary and reasonable to expect that the abundance of data collected by previous workers in this field over the past years should either support or deny it. That this concept is supported by the data of previous workers, if not by their analysis, is shown below.

In our series of 107 patients with chorea, forty-one (38 per cent) (thirty-one from Chart 1 and ten from Chart 2) had other manifestations of rheumatic infection. The percentage of patients with chorea who have shown other rheumatic manifestations has varied somewhat in the numerous studies which have been made. This is due in large part to the different manner in which the statistical data was organized in each study and to the criteria used by various investigators for the diagnosis of rheumatic fever. Nevertheless, in fourteen of the following twenty studies the percentage of other rheumatic manifestations in patients with chorea was below 50 per cent, yet almost all of these investigators concluded from this that chorea along with rheumatic arthritis is merely another manifestation of rheumatic fever. More striking, perhaps is the fact that of the 6,543 cases which these studies represent only 33 per cent showed other manifestations of rheumatic fever.

Thus Johnston[7] found other evidence of rheumatic fever in only 41 per cent of his seventy-one patients with chorea (leaving 59 per cent without other evidence of rheumatic infection); Gibson[8] found other evidence of rheumatic fever in 56 per cent of his 581 patients with chorea (leaving 44 per cent without other evidence of rheumatic infection); Sutton and Dodge[9] in 52 per cent of their 466 choreic patients (leaving 48 per cent without); Coburn and Moore[10] in 49.7 per cent of their 137 hospitalized choreic patients (50.3 per cent without); Parrish and associates[11] in 30.3 per cent of 112 patients (69.7 per cent without); Gerstley, Wile, and Falstein[12] in 13.3 per cent of 150 patients (86.7 per cent without); Schwarz and Leader[13] in 10.7 per cent of eight-four patients (89.3 per

cent without); Jones and Bland[14] in 72 per cent of 482 patients (28 per cent without); Mackie[15] in 13.4 per cent of eighty-nine patients (86.6 per cent without); Poynton and associates[16] in 64.4 per cent of 104 patients (35.6 per cent without); Abt and Levinson[17] in 16.7 per cent of 143 patients (83.3 per cent without); Helmholtz[18] in 21 per cent of 138 patients (79 per cent without); Starr[19] in 17 per cent of 2,239 patients (83 per cent without); Thayer[20] in 21.6 per cent of 808 patients (78.4 per cent without); Batten[21] in 53 per cent of 115 patients (47 per cent without); Holt[22] in 56.7 per cent of 111 patients (43.3 per cent without); Sachs[23] in 11.4 per cent of seventy patients (88.6 per cent without); Osler[24] in 27.2 per cent of 110 patients (72.8 per cent without); Mackenzie[25] in 32 per cent of 439 cases (68 per cent without); and West[26] in 37.6 per cent of ninety-three patients (62.4 per cent without). This carries the data back to 1874.

If the total number of cases listed above are added together, there are 6,543 cases, with 33 per cent showing other evidence of rheumatic disease, and 67 per cent showing no other evidence of this disease. In the light of our analysis it is our contention that these figures indicate that the generally accepted conclusion that chorea is a manifestation of rheumatic fever is not valid. It is quite obvious that the reverse of the present argument may be used, that is to say, 67 per cent do not have other supporting evidence of rheumatic fever, and therefore chorea is not always a manifestation of rheumatic fever.

Of the above authors, some did question the rheumatic nature of all cases of chorea. Notable among these were Gerstley, Wile, and Falstein[12] and Coburn and Moore.[10] However, chorea is still considered to be a manifestation of rheumatic fever; and it is thus described in the chapters on rheumatic fever in current texts. Sutton and Dodge[9] concluded that "chorea should continue to be regarded not only as a manifestation but as a major manifestation of rheumatic infection," although only 52 per cent of their 467 patients had other evidence of rheumatic infection. Furthermore, 71.9 per cent of their 585 patients with rheumatic fever without chorea developed rheumatic heart disease, but only 50 per cent of their 467 patients with chorea followed for six years developed rheumatic heart disease. Jones and Bland[14] concluded that chorea was "a mild manifestation of rheumatic fever." However, their data shows that 86 per cent of their 518 cases of rheumatic fever without chorea developed heart disease, whereas only 3 per cent of 134 choreic patients without other rheumatic manifestations developed heart disease. Their data also show that of 348 choreic patients *with* other rheumatic manifestations 73 per cent developed heart disease.

A review of the early history of this disease is also most revealing. In the eighteenth and early nineteenth centuries, chorea was considered to be due to psychic factors, especially fear.[27] Stoll[28] in 1780 was probably the first to report cases wherein chorea and rheumatic fever coexisted. However Roger,[29] in 1866, is generally credited with proving that chorea is a manifestation of rheumatic fever, and he refers to this association as a "loi pathologique." In Roger's day it was not generally known that rheumatic fever is common in

childhood, and that rheumatic fever is a cause of heart disease, let alone that chorea is often associated with rheumatic fever. As a pioneer and keen observer, Roger undertook to prove all of these relationships at once. In doing so, however, he reported eighty-seven patients[30] in his papers on chorea, all of which had rheumatic fever and most of which, but not all, had chorea. He did not know the total number of patients[31] from which he had selected these cases over a ten-year period, and he was not concerned with choreic patients who might not have rheumatic fever. He is therefore justly credited with proving the existence of an association between rheumatic fever and chorea; unfortunately, however, his convincing presentation led most subsequent observers to overlook the relatively large number of choreic patients who do not have rheumatic fever.

Only a few, such as Sturges,[32] called attention to the large group in which this association was not clear. During the years which followed the reports of Roger, Sturges[33] (1883), Hughes[34] (1846 and 1855), Gowers[35] (1898), Smith[36] (1886), and Sachs[37] (1905) still considered fright and other psychic factors to be very important, and they expressed dissatisfaction with the idea that rheumatic fever is the principal or sole cause of chorea. Nevertheless, prominent men such as Still[38] regarded chorea to be "just as good evidence of rheumatism as a gumma is of syphilis."

DISCUSSION AND CONCLUSION

From our data and from the above re-evaluation of the literature the following was concluded. Chorea associated with an increased erythrocyte sedimentation rate is in most instances a manifestation of active rheumatic fever. Patients, on the other hand, who have their first episode of chorea with a normal sedimentation rate (in the absence of cardiac failure) do not have rheumatic fever and are no more subject to its sequelae than are other members of the population. The subsequent incidence of rheumatic disease in these patients may be expected to be similar to that of the general child population.*

The etiology of nonrheumatic chorea is not established. The data of some of the earlier investigators, the seriousness of the psychic traumata and their temporal relationship to the onset of chorea in our nonrheumatic choreic patients in this series, and the fact that obvious emotional disturbances were more varied in character and more than twice as common in the nonrheumatic

*In this connection, the incidence of rheumatic fever in the child population is of importance. Since it is not a generally reported disease, adequate statistics are not available. In a recent study by Quinn,[39] the incidence was estimated by adding together those patients with mitral disease and those patients with "potential heart disease" and a history of rheumatic fever. From his study of 401 school children in Georgia, he thus estimated an incidence of two cases of rheumatic fever per 100 children. Of 442,763 school children examined in Chicago,[40] 6,011 were found to have organic heart disease. Eighty per cent of organic heart disease in this age group is considered by Paul and associates[41] to be due to rheumatic fever. On this basis, 4,809 children of this group had rheumatic heart disease. Inasmuch as more patients have rheumatic fever than have rheumatic heart disease, the incidence of rheumatic fever in Chicago children may be conservatively estimated to be more than 1 per cent. Thus, one would expect to find among 100 nonrheumatic choreic patients at least one who might later develop rheumatic fever, or who at one time had rheumatic fever with no chorea. It is this high incidence of rheumatic fever in the child population that most probably explains the one patient in this study who had a history of rheumatic fever with heart involvement but with no chorea, and who, after a free interval of four years, had one episode of chorea with a normal sedimentation rate. During this episode of chorea he had no clinical evidence of either active or inactive heart disease and no other evidence of rheumatic activity. (This case is not included on the charts.)

group than in the rheumatic group, suggest that psychogenic factors are particularly important in nonrheumatic chorea. Future experience with the modern psychotherapeutic approach in these cases may yield much practical information.

Recurrences of chorea may be seen in patients with rheumatic chorea or in those with nonrheumatic chorea. In patients whose first episode of chorea is nonrheumatic, the recurrences are also nonrheumatic. In patients whose first episode of chorea is rheumatic, the recurrences are most likely to be rheumatic; but occasionally they may be nonrheumatic, possibly on a psychogenic basis.*

This concept of chorea is of great practical importance, not only because it singles out more clearly those patients with chorea who require closer study for possible sequelae of rheumatic fever, but it is equally important because it enables the physician to distinguish between these and those patients with chorea who do not have rheumatic fever and who need not fear the sequelae of this disease.

SUMMARY

Sydenham's chorea may be associated with rheumatic fever, or it may be nonrheumatic. Evidence to support this is adduced not only from our own data, but also from a re-evaluation of the data of previously reported studies.

Patients with nonrheumatic chorea are no more subject to the sequelae of rheumatic fever than are other members of the population.

REFERENCES

1. Holt, L. E., and McIntosh, R.: Holt's Diseases of Infancy and Childhood, New York, 1940; D. Appleton Century Company, p. 1202.
2. Mitchell, A. G., and Nelson, W. E.: Textbook of Pediatrics. Phila., 1945, W. B. Saunders Company, p. 851.
3. Brennemann, J.: Practice of Pediatrics. Vol. II, Hagerstown, Maryland, 1945, W. F. Prior Company, Inc., Chapt. 19, p. 15.
4. Landau, A.: Microsedimentation (Linzenmeier-Raunert Method), Am. J. Dis. Child. **45**: 691, 1933.
5. Herzog, R. S..: The Microsedimentation Rate, J. Lab. & Clin. Med. **27**: 355, 1941.
6. Hughes, H. M.: Digest of 100 Cases of Chorea, Guy's Hosp. Rep., London. 2.s, **4**: 375, 1846.
7. Johnston, J. A.: Chorea, J. Mich. M. Soc. **45**: 202, 1946.
8. Gibson, S.: Brennemann's Practice of Pediatrics. Vol. II, Chapt. 19, p. 15, 1945.
9. Sutton, L. P., and Dodge, K.: The Relationship of Sydenham's Chorea to other Rheumatic Manifestations, Am. J. M. Sc. **195**: 656, 1938.
10. Coburn, A. F., and Moore, L. V.: The Independence of Chorea and Rheumatic Activity, Am. J. M. Sc. **193**: 1, 1937.
11. Parrish, P. S., Taran, L. M., and Starr, S.: The Incidence of Heart Disease in Cases of Sydenham's Chorea, J. PEDIAT. **11**: 617, 1937.
12. Gerstley, J. R., Wile, S. A., and Falstein, E. I.: Chorea: Is It a Manifestation of Rheumatic Fever? J. PEDIAT. **6**: 42, 1935.
13. Schwarz, H., and Leader, S. D.: Latent Cardiac Complications following Sydenham's Chorea, Am. J. Dis. Child. **49**: 952, 1935.
14. Jones, T. D., and Bland, E. F.: Clinical Significance of Chorea as a Manifestation of Rheumatic Fever, J. A. M. A. **105**: 571, 1935.
15. Mackie, T. T.: Rheumatic Fever. An Analytical Study of 393 Cases of Rheumatic Fever and 89 Cases of Chorea, Am. J. M. Sc. **172**: 199, 1926.

*Patients with rheumatic chorea may also have a persistence of their choreic signs after all other evidences of rheumatic activity have subsided and the sedimentation rate has become normal. The reason for the persistence of chorea in these patients is again not clear. Because of this, however, it is necessary to do sedimentation tests early in the illness to establish the diagnosis.

16. Poynton, F. J., Patterson, D., and Spence, J. C.: Acute Rheumatism in Children, Lancet **2**: 1086, 1920.
17. Abt, I., and Levinson, A.: A Study of 226 Cases of Chorea, J. A. M. A. **61**: 1342, 1916.
18. Helmholtz, H. F.: J. A. M. A. **61**: 1342, 1916.
19. Starr, M. A.: Organic and Functional Nervous Diseases, ed. 4, Philadelphia, 1913, Lea & Febiger, p. 778.
20. Thayer, W. S.: An Analysis of 808 Cases of Chorea, with Special Reference to Cardiovascular Manifestations, J. A. M. A. **47**: 1352, 1906.
21. Batten, F. E.: The Occurrence of Rheumatism in Children Subsequent to an Attack of Chorea, Lancet **2**: 1195, 1898.
22. Holt, L. E.: Diseases of Infancy and Childhood, New York, 1897, D. Appleton Century Company, p. 674.
23. Sachs, B.: Keating's Encyclopedia of Diseases of Childhood, Vol. IV, Philadelphia, 1890, J. B. Lippincott, p. 842.
24. Osler, W.: The Cardiac Relations of Chorea, Am. J. M. Sc. **188**: 371, 1887.
25. MacKenzie, S.: Report on Inquiry Nr. II, Chorea, Brit. M. J., p. 26, 1887.
26. West, C.: Lectures on Diseases of Infancy and Childhood, London, 1874, Longmans, Green and Company, p. 226.
27. Rufz, M.: Recherches sur quelques Points de l'Histoire de la Chorée chez les Enfants, Arch. Gen. de Med. II Serie, **4**: 215, 1834.
28. Stoll, M.: (a) Pars Tertia Rationis Medendi, Vienna, Austria. Vols. III-IV; Obs. 7, p. 414, Obs. 8, p. 416, 1780-89. (b) Pars Septima Rationis Medendi, Vienna, Austria. **7**: 6, 1790.
29. (a) Roger, H.: Recherches Cliniques sur la Chorée, sur la Rhumatisme et sur les Maladies du Coeur chez les Enfants. V Prem. Partie: Du Rhumatisme Articulaire et Visceral chez les Enfants, et Specialement de leur Rapports avec la Chorée. Arch. Gen. de Med. Vol. VIII: 8 iem Serie, pp. 641-665, 1866. (b) Recherches Cliniques sur le Rhumatisme et sur les Maladies du Coeur chez les Enfants. Arch. Gen. de Med. Vol. IX: 6 iem Serie, pp. 54-75, 1867. (c) Recherches Cliniques sur la Chorée, sur la Rhumatisme et sur les Maladies du Coeur chez les Enfants, et Specialement du leurs Rapports avec le Chorée (Chorée Cardiaque). Arch. Gen. de Med. Vol. XI: 6 iem Serie, pp. 26-42, 148-178, 288-305, 393-421, 1868.
30. See (29, c), p. 409.
31. See (29, c), p. 36.
32. Sturges, O.: School Work and Discipline as a Factor in Chorea, Lancet **1**: 9, 1885.
33. Sturges, O.: The Rheumatic Origin of Chorea, Lancet **2**: 808, 1883.
34. Hughes, H. M.: (a) See (6), pp. 360-395. (b) Hughes, H. M., and Brown, E. B.: Digest of 209 Additional Cases of Chorea, Guy's Hosp. Rep., London **1**: 3. 217, 1855.
35. Gowers, W. R.: A Manual of Diseases of the Nervous System, ed. 2, Philadelphia, 1898, P. Blakiston's Son and Company. Part V, pp. 592-628.
36. Smith, J. Lewis: Diseases of Infancy and Childhood, ed. 6, Diseases of the Cerebrospinal System, Philadelphia, 1886, Lea & Febiger, Chap. XIV, Part III, Sect. I, pp. 512-528.
37. Sachs, B.: A Treatise of Nervous Diseases of Children, ed. 2, New York, 1905, Wm. Wood, pp. 108-128.
38. Still, G. F.: Common Disorders of Diseases of Childhood, ed. 3, London, 1920, American Branch of the Oxford University Press, pp. 514-532.
39. Quinn, R. W.: The Incidence of Rheumatic Fever and Heart Disease in School Children in Dublin, Georgia, with some Epidemiological and Sociological Observations, Am. Heart J. **32**: 234, 1946.
40. Bull. Chicago Heart Association **5**: 8, 1927.
41. Paul, J. R., Harrison, E. R., Salinger, R., and DeForest, C. K.: The Social Incidence of Rheumatic Heart Disease, Am. J. M. Sc. **188**: 303, 1934.

A COMPARISON OF VITAMIN C IN MOTHERS AND THEIR PREMATURE NEWBORN INFANTS

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IN A recent report[1] we compared the mother's vitamin C with that of her full-term newborn infant by means of the intradermal test. The intradermal tests of the newborn infants and their mothers indicated that the newborn infants had a higher vitamin C tissue concentration than their mothers. These results were in substantial agreement with reports[2] of the neonatal-maternal plasma ascorbic acid relationship. Here, the plasma ascorbic acid concentration of the newborn infant has been shown to be considerably higher than that of the maternal blood. These similar results with both intradermal tests and blood levels have suggested the important concept that the fetus takes its supply of vitamin C and tends toward saturation, whether or not the mother has a sufficient amount.

We then proposed to compare the mother's vitamin C with that of her premature newborn infant. There have been few vitamin C studies in premature newborn infants. Steinebrei[3] did urine tests in prematures between 10 to 15 days of age (not soon after birth). He found less saturation than in normal newborns, but there was no connection between the degree of saturation and the body weight. An increase of vitamin C intake had no influence on the development of the premature infants. Levine and his co-workers,[4] in an excellent study, demonstrated that premature infants on vitamin C free cow's milk containing 5 Gm. or more of protein per kilogram, exhibited a spontaneous defect in the intermediary metabolism of aromatic amino acids. The administration of l-ascorbic acid completely eradicated the defect without necessarily raising the plasma ascorbic acid levels. Dann[5] found that premature infants receiving human milk retain a larger part of a "saturation dose" of ascorbic acid in their tissues than do infants given cow's milk. The hypothesis is offered that an increased daily requirement for vitamin C is related to a high level of protein intake.

PLAN OF STUDY

A comparison of the vitamin C in mothers and their premature newborn infants was to be made by means of the intradermal test.[6] This is a qualitative test based on the intradermal injection of a dye, which will be decolorized by vitamin C. A skin test time (time for disappearance of dye) of 14 minutes or more indicates a definite degree of tissue unsaturation; from 10 to 13 minutes is borderline, and less than 9 minutes a normal amount of vitamin C in the body tissues.

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This intradermal test was done in duplicate on mothers and their premature newborns, as soon after birth as possible. A number of the premature infants had tests at intervals during their entire stay in the hospital. During this time they were receiving various amounts of ascorbic acid. All of these premature infants received evaporated milk formulas. They also were given concentrated cod-liver oil and vitamin B complex.

RESULTS

The intradermal test for vitamin C was done on thirty premature newborn infants and their mothers. The first test was done as early as possible, within a few hours to one week after birth. The results are found in Table I.

TABLE I. THE FIRST INTRADERMAL TEST FOR VITAMIN C IN PREMATURE NEWBORN INFANTS AND THEIR MOTHERS

NO.	RACE	SEX	MONTH OF GESTATION	BIRTH WEIGHT (KG.)	INFANT'S AGE (DAYS)	TEST TIME (MIN.)	MOTHER AGE (YR.)		TEST TIME (MIN.)
1	N	F	8½	2.27	5	4.8	19		18.0
2	W	M	8½	2.44	2	6.6	23		15.9
3	W	M	7	1.79	0	5.1	22		15.3
4	W	M	7	1.30	3	3.6	19		14.4
5	N	M	8	2.25	5*	4.5	26		13.8
6	W	F	8	1.62	5	5.2	29		13.4
7	W	F	7	1.25	1	4.9	23		12.9
8	W	F	7	2.35	1	3.4	33		12.9
9	W	F	7	1.72	1	4.9	28		12.6
10	W	M	7	1.52	1	3.5	22	twins	12.2
11	W	M	7	1.13	1	6.6	22		12.2
12	W	M	7	2.01	1	3.3	26		11.8
13	W	M	8½	2.18	4	4.7	26		11.1
14	N	F	8½	2.27	0	4.0	34		11.0
15	N	F	7	1.77	5	4.9	21		9.9
16	N	F	8	2.50	1	5.5	33		9.6
17	W	F	7	1.76	2	4.8	23		8.9
18	W	F	8	2.10	3	5.0	19		8.5
19	W	F	7	1.10	6	3.7	28		8.4
20	N	F	8	2.10	3	4.2	37		8.2
21	N	F	7½	1.84	1	3.6	16		8.1
22	N	M	7	2.07	1	2.6	22		7.9
23	W	F	8	1.96	0	9.5	38		7.5
24	W	F	8	2.31	0	7.0	28	twins	7.0
25	W	F	8	1.96	0	6.6	28		7.0
26	W	M	8	2.16	1	4.3	18		5.9
27	W	F	7	1.90	2	4.9	35		5.6
28	W	F	8½	2.01	5*	4.3	28		5.6
29	W	M	6½	1.30	7	3.3	—		—
30	N	F	7	2.13	6	6.1	—		—

*50 mg. vitamin C daily.

The intradermal test times for disappearance of the dye were shorter in the premature newborn infant than in the mother except in one instance. The average intradermal test time for the premature newborn infants was 4.9 minutes, and for their mothers 9.1 minutes. The weight of the infant had no relationship to the test time.

Ten of the premature newborn infants were followed for about eight weeks after birth. Each baby was given from 25 to 100 mg. of ascorbic acid daily. An intradermal skin test for vitamin C was done weekly. The weights were taken every other day.

The results are found in Table II. The intradermal test times indicated a good vitamin C concentration in the tissues in all the prematures throughout the study. Prematures who received 25 mg. of ascorbic acid daily had test times which compared favorably with those taking large doses. All the prematures gained weight. We had the impression clinically that the prematures receiving 50 mg. or more daily gained better than those receiving 25 mg. This could not be confirmed statistically in a small series such as this.

COMMENT

The average intradermal test time for the mothers of the premature newborn infants was 9.1 minutes. In a previous study of seventy-seven mothers of normal newborn infants, the average intradermal test time was 9.4 minutes. These similar figures contradict Jaroschka's[7] suggestion that vitamin C deficiency of the mother has a role in the occurrence of premature births.

The average intradermal test time for the premature newborn infants was 4.9 minutes and for the 77 full-term newborn infants, 5.0 minutes. The maternal-full-term newborn relationship was thus very similar to that of the maternal-premature newborn infant. As in our previous series, even where mothers were depleted of vitamin C, the premature newborn infants had a good tissue concentration. For example, in Case 1, the mother's intradermal test time for disappearance of the dye was 18 minutes and the premature's was 4.8 minutes.

It is difficult to explain how the premature and full-term newborn infants achieve good vitamin C tissue concentration even when their mothers are depleted. Lund and Kimble[2c] have presented good evidence that the placenta acts selectively to retain the vitamin C in the fetus. To add to this concept, we have suggested that the fetal nervous-humoral control for vitamin C is set at a higher level than that of the mother.

Since the intradermal test is qualitative rather than quantitative, we cannot say definitely that the premature has the same body stores of vitamin C at birth as the normal newborn infant. However, in preliminary blood studies of thiamine, which is also a water soluble vitamin, the premature seems to have as good a concentration as the normal newborn.

In view of the work of Levine and his associates,[4] and since the premature does have a more rapid metabolism than the full-term newborn infant, it would be wise in the present state of our knowledge to start ascorbic acid early, probably in the first week of life. The follow-up of the ten prematures indicates that 50 mg. of ascorbic acid daily gives good tissue concentrations of vitamin C.

SUMMARY

1. A comparison of the vitamin C in mothers and their premature newborn infants was made by means of the intradermal test.

2. The average intradermal test time for premature newborn infants was 4.9 minutes, and for their mothers, 9.1 minutes. This was similar to the full-term newborn-maternal relationship.

TABLE II. FOLLOW-UP ON TEN PREMATURE INFANTS

CASE	RACE	SEX	MONTH OF GESTATION	BIRTH WEIGHT (KG.)	1ST VITAMIN C DETERMINATION: AGE (DAYS)	1ST VITAMIN C DETERMINATION: TEST TIME (MIN.)	WEEKS AFTER BIRTH: 1	2	3	4	5	6	7	8	
1	W	F	7		1	4.9	2.6	5.0	3.5	2.7	3.4	3.4	3.9		Skin test time (min.)
				1.25		1.25	1.25	1.15	1.53	1.75	1.99	2.25	2.44		Weight (kg.)
								50	50	50	50	50	50		A. A. Adm.* (mg.)
2	W	F	8		3	5.0	6.7	5.7	4.3	4.1	5.5	3.7	5.4	4.7	Skin test time (min.)
				2.10		1.80	1.80	1.90	2.16	2.20	2.38	2.59	2.70	2.78	Weight (kg.)
										25	25	25	25	25	A. A. Adm. (mg.)
3	N	F	7		0	4.9	4.8	2.6	3.9	5.2	3.2	4.4	4.7	4.0	Skin test time (min.)
				1.77		1.77	1.59	1.72	1.90	2.00	2.07	2.25	2.52	2.92	Weight (kg.)
						50	50	50	50	50	50	50	50	50	A. A. Adm. (mg.)
4	W	F	7		1	4.9	5.0	3.5	3.0	2.3	4.5	5.1	5.1	4.5	Skin test time (min.)
				1.72		1.72	1.75	1.84	2.04	2.10	2.21	2.27	2.35	2.47	Weight (kg.)
									25	50	50	50	50	50	A. A. Adm. (mg.)
5	W	M	7		0	5.1	6.0	4.9	3.9	3.1	3.0	1.9			Skin test time (min.)
				1.79		1.79	1.46	1.56	1.90	1.97	2.04	2.37			Weight (kg.)
								25	25	25	100	100			A. A. Adm. (mg.)
6	W	M	7		1	3.3	3.7	3.3	3.2	3.0	3.2	2.1			Skin test time (min.)
				2.01		1.97	2.00	2.00	2.04	2.35	2.50	2.72			Weight (kg.)
								25	25	25	100	100			A. A. Adm. (mg.)
7	W	F	7		2	4.8	4.8	4.4	6.1	4.4	3.7	3.9	2.8	4.6	Skin test time (min.)
				1.76		1.68	1.75	1.81	1.92	2.10	2.25	2.50	3.00	3.86	Weight (kg.)
							50	50	50	100	100	100	100	100	A. A. Adm. (mg.)
8	W	F	8		5	5.2	5.2	2.8	4.2	2.3	3.7	3.0	4.8	2.8	Skin test time (min.)
				1.62		1.50	1.60	1.74	1.95	2.18	2.35	2.67	2.80	2.92	Weight (kg.)
							100	100	100	100	100	100	100	100	A. A. Adm. (mg.)
9	W	F	8½		5	4.3	4.3	4.2	3.9	4.0	2.7				Skin test time (min.)
				2.01		1.97	2.08	2.21	2.38	2.68	3.06				Weight (kg.)
						50	100	100	100	100	100				A. A. Adm. (mg.)
10	N	M	8		5	4.5	4.5	4.6	6.0	7.6	5.8				Skin test time (min.)
				2.25		2.07	2.08	2.18	2.41	2.71	3.06				Weight (kg.)
						50	100	100	100	100	100				A. A. Adm. (mg.)

*A. A. Adm. = ascorbic acid administration.

3. The premature, like the full-term newborn, has a good vitamin C level at birth even where the mother is depleted.

4. 50 mg. of ascorbic acid daily begun in the first week insures continued good tissue concentrations of vitamin C.

REFERENCES

1. Slobody, L. B., Benson, R. A., and Mestern, J.: J. PEDIAT. **29:** 41, 1946.
2a. Concepcion, I., and Camara, S.: J. Philippine Islands M. A. **19:** 139, 1939.
b. McDevitt, E., Dove, M., Dove, R., and Wright, I.: Proc. Soc. Exper. Biol. & Med. **51:** 289, 1942.
c. Lund, C., and Kimble, M. S.: Am. J. Obst. & Gynec. **46:** 635, 1943.
d. Snelling, C. E., and Jackson, S. H.: J. PEDIAT. **14:** 447, 1939.
e. Manahan, C. P., and Eastman, N. J.: Bull. Johns Hopkins Hosp. **62:** 478, 1938.
f. Wahren, H., and Rundquist, O.: Klin. Wchnschr. **16:** 1498, 1937.
g. Braestrup, P. W.: Acta paediat. **19:** 328, 1937.
h. Montero Sierra, B.: Rev. Chilena de pediat. **11:** 815, 1940.
3. Steinebrei, H.: Klin. Wchnschr. **18:** 489, 1939.
4. Levine, S. Z., Gordon, H. H., and Marples, E.: J. Clin. Investigation **20:** 209, 1941.
5. Dann, M.: J. Clin. Investigation **21:** 139, 1942.
6. Slobody, L. B.: J. Lab. & Clin. Med. **29:** 464, 1944.
7. Jaroschka, K.: München. Med. Wchnschr. **85:** 1871, 1938.

PSYCHIATRIC SERVICES IN A CHILDREN'S HOSPITAL

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THE advantages of psychiatric services in a general children's hospital are numerous and merit serious consideration. They appear to be in at least three categories: (1) the possible improvement of hospital care to the patients and their families; (2) the opportunities for increasing the quality and amount of psychiatric training of future pediatricians; and (3) the tremendous opportunities for research which would redound to the advancement of knowledge in not merely pediatrics but general psychiatry, and to the current interest in what is variously known as "psychosomatic" or "integral" medicine.

Each of these categories is a large and important field. They are obviously interdependent, and growth and development in any one would be reflected in, and enhance the growth and development of, the other two. Systematic and exhaustive discussion of any one would be difficult in view of space and time limitation here. But perhaps a few comments regarding each may still indicate the scope of the possibilities.

Concerning the need of psychiatric consultation service in a children's hospital perhaps not much needs to be said. The number of lonely, anxious, homesick children, and the number of aggressive, hyperactive children whose personality problems interfere with adequate treatment of whatever organic illness brings them to the hospital, is familiar to all experienced pediatricians. The neurotic components in such conditions as diabetes, cardiac diseases, epilepsy, metabolic disorders, the obesities, and the anorexias are also sufficiently well known. The host of allergic disorders of the respiratory and the gastrointestinal tracts, of the skin, and perhaps of other systems are by now of common interest to the pediatrician as well as the psychiatrist. The need for further study of the psychogenic factors in the choreas and in the nutritional disorders of infancy and early childhood is indicated by recent reseach.[1] The proportion of serious emotional reactions of children to various surgical procedures are probably as well known to the pediatrician as to the child psychiatrist. That the treatment of all these clinical problems in a children's hospital may be improved to the end that not only the current illness may be less complicated, but also that the personality development of the child may be fostered, is a desire of every pediatrician of experience.

Spock[2] and others have emphasized the critically important role and the strategic position of the pediatrician in furthering this goal of mental hygiene of the young and of future generations. It is not at all an exaggeration to say that the pediatrician may contribute more to this goal than the psychiatrist. Hence, there is growing interest of departments of pediatrics in our medical schools to give at least some psychiatric experience and training to future pediatricians. In a children's hospital with a well-organized psychiatric service, the

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resident pediatrician might obtain such training not, as now in some training centers, for short periods of a few months on a psychiatric hospital ward for children, but more or less continuously throughout his residency. Psychiatric training in my opinion is not merely the acquisition of information about the classically described syndromes of psychoses and psychoneuroses, but is even more importantly a matter of acquiring a therapeutic attitude toward all emotional difficulties of people. Hence, time and exposure to trained personnel is essential to prevent compartmentalization of such knowledge and skill in the young pediatrician's mind. Furthermore, demonstration of the importance of the affective and the personal elements in all diseases by the psychiatric service will be a much more effective training method. It is perhaps not too much to expect also that the senior visiting staff of pediatricians might benefit and fill some gaps in their own training as a result of the participation of psychiatric personnel in the total treatment. One cannot omit either the advantages accruing to psychiatrists from the closer contact and collaboration with the pediatrician that integrating the psychiatric service into such a hospital would make possible.

The research that such collaboration would permit appears to be of inestimable scope. General psychiatric theory as to the genesis of personality traits and of personality disorder would obtain still another opportunity for testing and elaboration. Numerous questions need more intensive and detailed study. One question, for example, is the dynamism of repression of impulses of the infantile period as against their healthier integration into the self of the child and factors involved in each. The genesis of many somatic disorders now suspected of having large psychological components in their etiology and maintenance could be further explored. The obesities, the chronic states of malnutrition, the asthmas, the various vegetative instabilities, including hypertention, gastric disorders, and many others which express the anxiety of the individual, are a few of the conditions which come to mind. Necessarily, methods of treatment could be further refined and perhaps principles, upon which more effective hygiene and preventive programs could be based, might be derived. The value, content, and form of group prenatal preparation of mothers for the job of child rearing might be studied. The value of educational programs of various types via written word, radio, and visual-aid methods could be tested. The changes in methods of infant nursing during the confinement of the mother in the hospital as suggested by The Cornelian Corner,[3] together with further education of the obstetricians, would certainly be of great importance.

Concerning the general organization of such psychiatric services in a pediatric hospital one might consider two general possibilities. One of these is the establishment within the hospital of a ward or two for the patients of the psychiatric department. The other is to assign no actual bed space to the psychiatric department, but only office space for its personnel and rooms suitably equipped for their examinations and for play or interview therapy. There come to mind advantages and disadvantages to both plans, and local conditions, preferences, and purposes would be decisive. Against the first-mentioned plan are the considerations that this might be a duplication of other facilities in the

community, that perhaps although geographic distances might be reduced, there would still remain some isolation or separation of the psychiatric service from the rest of the hospital. There may be other objections. Against the second plan, on the one hand, there might arise the argument that without its own bed facilities, other necessary space and responsibility for its own nursing and attendant personnel, the psychiatric department might be somewhat hampered in its function of demonstrating and teaching its methods of treatment to the rest of the hospital staff. Specific research programs of the psychiatric staff might be impeded. Furthermore, the department's status and prestige, not unimportant considerations, within the hospital organization might suffer. On the other hand, if this latter problem were otherwise met, the efforts of the psychiatric service might then be channeled and diffused throughout the hospital personnel. If, for example, the recreational, occupational, and educational personnel were subordinated to the psychiatric service; if all nursing and resident staff were regularly indoctrinated, trained by, and recognized the responsibility of, the psychiatric services in the personal or emotional aspects of the child's adjustment to the hospital, some of its essential functions could then be performed.

The personnel of such a psychiatric service could easily be adapted from that of out-patient psychiatric clinics for children or from that of a child psychiatry department of a general psychiatric hospital. In both situations it consists of a time-tested, basic, clinical team composed of psychiatrist, psychiatric social worker, and clinical psychologist all trained in psychotherapeutic work with children and their parents. It is necessary to emphasize the qualification of training and experience in psychotherapeutic work with children and their parents. General psychiatric hospital training, even Specialty Board certification for the psychiatrist, has been amply proved by experience to be insufficient preparation for psychiatric work with children. A psychiatrist without thorough training in psychotherapeutic techniques with both children and adults is less well qualified if only because he is unprepared to treat (and therefore unprepared to teach pediatric residents how to treat) at least one half of the problem, namely, the conflicts of the parent. It is by now well established that advice, suggestions, and reassurance, not based on, or directed by, precise psychodynamic orientation, are of little use to either the parent or the child in the solution of their common and mutual problems. It is by now clear that psychiatrists untrained and inexperienced in the long, intensive, and detailed psychotherapy necessary are very apt to resign from chronic or severe psychogenic disorders by assigning the etiology to the unproved realms of the idiopathic organic, constitutional, or hereditary categories. Such psychiatrists find themselves in the unenviable position of being unable to give either leadership to their own ancillary nonmedical staff or help to their nonpsychiatric medical colleagues.

Similar considerations hold true for the psychiatric social worker and clinical psychologist members of the psychiatric team. If neither of these has had therapeutic experience with children *and their parents* the clinical efficacy of

their combined efforts is reduced. Experience in a state or other mental hospital for adults in obtaining social histories from relatives, doing follow-up studies upon patients after discharge, or performing other social case-work functions is not enough for the psychiatric social worker. She may too often, in the team contemplated, be called upon to deal therapeutically under the psychiatrist's supervision with one or another person of the family and perhaps even with the child himself if the parent presents the more formidable therapeutic problem requiring the psychiatrist's personal attention. As for the clinical psychologist, he, too, is less useful if his chief contribution consists of psychometry, educational and personality testing even if combined with the more modern projective techniques. Conceivably, if the psychologist is used for routine group or individual tests largely for diagnostic purposes, and perhaps for selecting patients requiring closer and fuller psychiatric scrutiny, then the therapeutic skills might be expected in the other two members of the team. Finally, it cannot be overemphasized that research and teaching prospects will vary directly as the psychotherapeutic skill of the psychiatric staff.

Another possibility in this connection is that all the social service workers of a hospital might either be psychiatrically trained, as outlined previously, or at least be administratively connected with the psychiatric services. This would ensure, or at least increase the probability that all work by the social workers with parents, other relatives, and the community will be integrated with the rest of the treatment, and that pertinent data will be collated for research, teaching, and treatment.

One cannot leave the problem of the psychiatric personnel without one or two comments regarding the nurses, attendants, and other specialists having contact with the patients, such as teachers, occupational and physical therapists, and recreation workers. Recent studies[4] are emphasizing the importance, in the total treatment of the child in the hospital, of the attitudes of such persons who may have closer and longer contact with the patients than either the resident or attending physicians. Pertinent here are not only the matter of selection of the emotionally relatively healthy for such staff positions, but also the need for regular inclusion of this portion of the staff in general discussions, conferences, and planning of treatment. Clearly and without ambivalence, to give recognition to their psychotherapeutic potentialities in such ways is being found to bring rich rewards in clinical results. All experienced clinicians know, but perhaps do not consistently make use of the knowledge, that the attitude and personality of the nurse is of crucial importance at times in the progress of the patient.

In conclusion, one can just hint at other problems and possibilities which result from integrating psychiatric services in a children's hospital. There is the need to work out methods of helping overburdened and frequently overanxious and oversolicitous mothers of the chronically ill child. The various debilitating or handicapping prolonged illnesses are often important factors in the psychological crippling of the child and in the enslavement of parents who must repress the understandable hatreds with resulting anxieties, self-criticism, and uncertainty in meeting the child's actual emotional needs. There is the possi-

bility of doing still more effective mental hygiene and preventive psychiatry in well-baby clinics or in out-patient prenatal clinics (if these are included in such a children's hospital) by the relief of the numerous and common anxieties of mothers of infants and of prospective mothers.

Finally, to return to a previous point, the more thorough supervision and training of the resident pediatrician in such psychotherapeutic techniques as every physician can learn may be perhaps the most important contribution of modern psychiatry in the children's hospital to the generations that follow. Perhaps in such ways the life-long distortions of physiology and character by the culture-bearers, the predominantly neurotic parents of the present, may be somewhat ameliorated, and future generations may, perhaps, be somewhat better prepared emotionally to order their world more sanely than have we or our forbears.

REFERENCES

1. Ribble, Margaret: The Rights of Infants, New York, 1943, Columbia Univ. Press.
Hilgard, Josephine R., and Szurek, S. A.: The Successful Psychotherapy of a Choreic Syndrome, Psychosom. Med. 5: 293, 1943.
2. Spock, Benjamin and Huschka, Mabel: The Psychological Aspects of Pediatric Practice. Pract. Libr. Med. and Surg. 13: 757, New York, 1938, D. Appleton-Century Co.
3. Moloney, James Clark, Montgomery, John C., and Trainham, Genevieve: The Newborn, His Family and the Modern Hospital, The Modern Hospital 67: 43, 1946.
4. A Round Table on Institutional Treatment of Children at Annual Meeting of Am. Orthopsychiat. Assn. at Cincinnati, Feb. 1947, with papers contributed by Helen Sutton, Anne R. Benjamin, and Howard E. Weatherly, Bruno Bettelheim, and S. A. Szurek, J. Orthopsychiat. Assn. of 1947 or 1948, to be published.

Case Reports

ABDOMINAL ABSCESS AS A CAUSE OF INTESTINAL OBSTRUCTION IN THE NEWBORN INFANT

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IN A recent review of congenital lesions resulting in surgical conditions of the abdomen, it is correctly stated that "the majority of serious maladies of early infancy are due to mechanical lesions or congenital lesions of a mechanical nature rather than any histopathologic alteration such as neoplasia or a primary inflammatory process."[1] We believe, therefore, that our recent experience with a newborn infant manifesting an inflammatory process in the form of an abdominal abscess resulting in intestinal obstruction is sufficiently unusual to warrant reporting.

CASE REPORT

A white male infant was transferred to our service on the fourth day of life because of an abdominal mass. The past history revealed that the infant was delivered spontaneously after a full-term gestation. The only significant prenatal history elicited was the occurrence of mild icterus of several days' duration in the mother during the fifth month of pregnancy. Recovery from the icterus was uneventful without any therapy and the obstetrician regarded the attack as a mild case of infectious hepatitis with no sequelae.

Physical examination of the infant on the first day of life revealed no abnormalities other than a large midabdominal mass. Inasmuch as the mass was not producing any symptoms, the infant was managed as a normal newborn. Breast feedings were well taken and retained; normal appearing meconium stools were passed. On the fourth day of life it was decided to transfer the infant to our service for further study.

Approximately one hour after admission to our service the infant developed severe vomiting which soon became fecal. No stools were passed at this time. Physical examination disclosed a well-nourished infant with marked abdominal distention. Dehydration was moderate. A large cystic mass which measured approximately 9 cm. in diameter was palpated in the midabdomen, the umbilicus being in the approximate center of the mass. It seemed directly under and attached to the anterior abdominal wall, but extended so deeply into the abdomen that the posterior wall could not be palpated.

A roentgenogram of the abdomen disclosed distended intestinal loops in the left abdomen and a short vertical "ladder" pattern of small intestinal obstruction (Fig. 1). The hemogram was as follows: 13.9 Gm. hemoglobin per 100 c.c.; 3,900,000 red blood cells per cubic millimeter; 10,000 white blood cells per cubic millimeter, with a differential count of 35 per cent neutrophiles, 5 per cent monocytes, and 60 per cent lymphocytes. The hematocrit was 38 mm. and the sedimentation rate was 8 mm. per hour (Wintrobe). The serum chlorides were within normal limits.

Decompression of the intestinal distention was promptly effected by continuous suction applied to a Levine tube which had been passed into the stomach. Twelve hours following admission the infant passed a small yellowish stool

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which was followed by six similar stools within the next twelve hours. None of these were positive for blood to the benzidine test.

Since the abdominal mass persisted following relief of the obstruction, it was believed advisable to undertake surgical exploration because of the possibility of recurrent intestinal obstruction. After adequate hydration by administration of intravenous fluids the patient was operated on by Dr. Warren H. Cole who made the following operative note:

"A midline incision was made, which included the umbilicus. Upon entry into the abdominal cavity the mass could be visualized and was seen to consist of numerous loops of small bowel bound to a cystic mass composed of fibrinous material of no definite structure. The interior of this cystlike cavity contained a small amount of clear yellowish fluid and underlying this a thick gummy layer of purulent material. Cultures were taken and a portion of the cystlike wall was sent to the pathology department for examination. The cyst was marsupialized to the anterior abdominal wall."

Fig. 1.—Roentgenogram illustrating distended loops in the left abdomen at the time of intestinal obstruction. A short vertical "ladder" pattern of small intestinal obstruction is also present.

Microscopic examination revealed that the cyst wall in some areas was a structureless mass of necrotic fibrin with polymorphonuclear and round cell infiltration and in other areas it was in contact with the anterior abdominal wall where there was an inner layer of fibropurulent exudate adjacent to a layer of granulation tissue with considerable fibrosis, round cell infiltration, numerous areas of calcification, and some deposition of yellow pigment.

Culture of the purulent material from this cystlike cavity demonstrated *Escherichia coli* the day following surgery. Consequently, streptomycin therapy, 60 mg. every three hours, was instituted in place of penicillin therapy, which had been administered following surgery. Sulfadiazine was given concurrently in doses of 0.1 Gm. every four hours. Blood transfusions, plasma, and fluids were given as supportive measures.

The operative wound healed well with no evidence of infection. Gradual oral feedings were begun on the third postoperative day and were gradually increased to full feedings during the following three days. The infant has now been observed six months postoperatively and has been entirely asymptomatic, manifesting entirely normal physical and mental development.

COMMENT

Intestinal obstruction in the newborn infant is most frequently caused by congenital anomalies. It was our impression preoperatively that we would encounter an omphalomesenteric cyst about which there had been some torsion of intestinal loops with resultant obstruction. When the mass was incised, however, it was obvious that it was not a simple cyst, but we still considered the possibility that it was an infected omphalomesenteric cyst. Careful inspection of the wall of the mass both grossly and microscopically failed to indicate any semblance of a cystic lining, suggesting that it probably was a pyogenic infection which had localized and become encysted by an inflammatory wall.

The precise time of onset of the inflammatory processs could not be ascertained, but the essential point of interest is the fact that it unquestionably had its origin during fetal life, inasmuch as it was observed on the first day of life. Its appearance and degree of localization also indicated that it was a process of relatively long duration. The culture of *Esch. coli* from the abscess suggests that this organism might well have been an invader during fetal life, which localized intra-abdominally, since there was no evidence to suggest postnatal contamination of the mass as might have occurred if the mass communicated with the intestinal lumen.

Since Simpson[2] reported a series of cases of fetal peritonitis in 1838 and reviewed the literature on the subject, numerous additional reports have appeared. Dubler[3] reported an abdominal cyst in a newborn infant which he believed due to an intrauterine perforation of the descending colon with resultant escape of meconium and consequent localization by fibrous adhesions and calcifications. Others[4-8] have reported cases of fetal peritonitis as a result of intestinal perforations and escape of meconium from the intestine. The phenomena arising as a result of meconium entering the peritoneal cavity have been described[8] as a reaction of the peritoneum to chemical and foreign body irritation with eventual formation of dense adhesions and calcified plaques. While it is not possible to state with absolute certainty that intestinal perforation and meconium peritonitis did not occur in our patient, this explanation for the abscess would not explain the culture of *Esch. coli* from the abscess without a demonstrable communication with the intestinal lumen.

It seems justifiable to speculate, therefore, that transplacental transmission of the organism occurred with the development of fetal peritonitis and ultimate localization with abscess formation. This possibility has been mentioned by Doran[9] and Abt.[10] No evidence of a maternal *Esch. coli* bacteremia could be established in retrospect, however, unless the brief maternal icterus was associated with bacterial invasion.

The postoperative course of our patient was uneventful. Although there has been no recurrence of the intestinal obstruction, this possibility exists because of the attachment of many intestinal loops to the abscess wall, which was marsupialized.

SUMMARY

An unusual case of intestinal obstruction in the newborn caused by an intra-abdominal abscess is presented. This abscess had its origin during fetal life.

REFERENCES

1. Mayo, C. W., and Remington, J. H.: Am. J. Surg. **72**: 841, 1946.
2. Simpson, J. V.: Edinburgh Med. and Surg. J. **15**: 390, 1838.
3. Dubler, A.: Virchows Arch. f. path. Anat. **111**: 567, 1888.
4. Falkenheim, and Alkanazy, M.: Jahrb. f. Kinderh. **34**: 71, 1892.
5. Zillner, E.: Virchows Arch. f. path. Anat. **96**: 307, 1884.
6. Paltauf, A.: Virchows Arch. f. path. Anat. **111**: 461, 1888.
7. Rudnew, W.: Inaugural Dissertation, Basel, 1915 (cited by Boikan[8]).
8. Boikan, W. S.: Arch. Path. **9**: 1164, 1930.
9. Doran, A.: Proc. Roy. Soc. Med., London **7**: 261, 1913-14.
10. Abt, Isaac A.: M. Clin. North America **15**: 611, 1931.

COOLEY'S ERYTHROBLASTIC ANEMIA IN TWO CHINESE BOYS

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THE erythroblastic anemia which Cooley described in 1927[1] was characterized by splenomegaly, bone changes, leucocytosis, and a progressive, hemolytic, hypochromic anemia with many erythroblasts. A normal or decreased fragility of the red cells in hypotonic saline was also a constant finding. Subsequent cases reported showed this anemia to afflict consistently children with Greek, Italian, or Syrian forebears, and led to the opinion that it occurred only in individuals of Mediterranean stock. This racial incidence had also been observed in a latent form of the anemia in adults. Smith[2] studied sixteen families of Mediterranean origin in which Cooley's anemia had been found. He revealed abnormalities of the blood characteristic of the anemia in fifty-four of the sixty-three persons examined. Occasionally, this mild form in adults is associated with splenomegaly as well as the symptoms of anemia.[3]

The term Mediterranean anemia has been applied to this blood dyscrasia because of its prevalence in the offspring of families native to lands bounding the Mediterranean Sea. Valentine and Neel[4] have suggested the terminology of thalassemia major and thalassemia minor to differentiate between the acute fatal form and the latent subclinical form of the disease.[4]

Cooley, Smith, and others who have investigated this anemia, have not held the opinion that it is race limited, although the disease is familial and appears to follow mendelian laws of inheritance. Cooley[5] early considered the anemia the result of a mutation whose characteristics were strengthened by consanguinuity. The mutation could account for the sudden appearance of the anemia in a person of any race anywhere in the world.

A case of Cooley's anemia has been reported in an English child,[6] and five cases in Asiatic Indian children.[7] Dameshek[8] mentioned a case seen in a Negro child in New York City. Foster[9] reported a female child of Chinese parentage born in Hawaii who had Cooley's anemia.

Three cases of hemolytic anemia with erythroblastemia were seen in Chinese infants at Peiping Union Hospital.[10] All had splenomegaly, microcytic hypochromic anemia, and leucocytosis. The cell fragility, however, was increased in all three cases. The first case responded to iron therapy. Skull roentgenograms revealed thickening of the tables of the frontal bones, but fasculation was absent. These cases therefore, do not fit Cooley's criteria.

Two cases of Cooley's anemia in Chinese boys, not related, have been observed at St. Vincent's Hospital in New York City. One child survived a splenectomy for three years and ten months. The second child, a more recent patient, is being maintained on blood transfusions.

REPORT OF CASES

CASE 1.—(Reported through the courtesy of Dr. Edwin DiTolla, who referred the patient to hospital.) K. L., an 8-month-old Chinese male infant, was first admitted to St. Vincent's Hospital on Oct. 14, 1941. His mother reported failure to gain weight and a noticeable pallor.

The mother had a normal delivery following an uneventful pregnancy. The child's birth weight was 6 lb., 3 oz. He received breast feedings supplemented

From the Pediatric Service of St. Vincent's Hospital, New York, Dr. Stanley Brady, director.

by a boiled whole milk formula, orange juice, cod liver oil concentrate, and, at about 3 months, cereal and puréed vegetables.

For the three months previous the mother thought the baby was becoming weak, sickly, and pale, and his appetite had become poor. He would hold up his head, but did not sit up and had no teeth.

The baby's father was a 36-year-old American-born Chinese who was employed as a clerk in a Chinese grocery. The mother, 23 years old and born in China, came to this country one year previously for her marriage as prearranged by her family. The mother had hay fever; the father had no complaints. No history of familial diseases was elicited. There were no known tuberculosis contacts. One sibling, a 20-month-old girl, was in good health.

On physical examination, the baby appeared about the stated age, well developed, fairly well nourished, and in no acute distress. He weighed 14 lb., 15 oz. The skin was sallow, and lips and mucous membranes were pale, but there was no cyanosis or icterus. The head was normal in shape, the fontanelles open. The heart showed questionable enlargement to both the left and right. There was a loud systolic murmur over the whole precordium, heard best at the apex. The heart sounds were of good quality, with the pulmonary second sound louder than the aortic second sound.

The abdomen showed slight distention. The spleen was hard, well outlined, sharp-edged, smooth, and nontender, extending from the left costal margin to a point 2 cm. below the umbilicus. The liver was a more indefinite mass palpable from the right parasternal line to the right anterior axillary line, about 3 cm. below the costal margin. No other masses, herniae, or areas of tenderness were palpated.

The blood count showed 10,100 white blood cells with 26 per cent neutrophiles, 70 per cent lymphocytes, and 4 per cent monocytes, with many large, toxic, unclassified forms noted. The red cell count was 2,490,000 with 5 Gm. of hemoglobin. The anemia was hypochromic, microcytic in type, with erythroblasts, normoblasts, basophilic stippling, and many Cabot's ring bodies. Marked anisocytosis and poikilocytosis were present. Repeated blood counts were essentially similar. The platelets ranged from 60,000 to 105,000 per cubic millimeter, and there was no evidence of sickling. The blood was type B, Kahn negative. The sugar was 82 mg., chlorides 579 mg., urea nitrogen 15 mg., phosphorus 6 mg., calcium 10.7 mg., and serum bilirubin 3.9 mg. per 100 c.c. of blood. The coagulation time was four minutes, and the bleeding time two minutes. A fragility test showed hemolysis beginning at 0.48 per cent saline and being complete at 0.32 per cent, compared with a control beginning at 0.46 per cent and being complete at 0.36 per cent.

A sternal puncture for bone marrow study revealed 4 per cent myeloblasts, 28 per cent myelocytes, 9 per cent metamyelocytes I, 28 per cent metamyelocytes II, 26 per cent polymorphonuclears, 2 per cent eosinophiles, 3 per cent reticulum cells, and nucleated red blood cells (60 normoblasts, 108 erythroblasts, 7 megaloblasts, and 4 unidentified). In about 70 per cent of the erythroblasts, the cytoplasm was observed as heavy, irregular, blue-staining granules.

The urine was positive directly for bilirubin and positive for urobilinogen in a 1:160 dilution and negative in a 1:320 dilution.

On admission, roentgenograms of the skull showed no distinct bone changes that could be associated with anemia. The long bones showed a slight degree of atrophy of the medullary portions with a tendency to thinning of the cortex. There was also a tendency to condensation of the distal ends of the diaphysis with less than the usual degree of flaring.

The diagnosis of Cooley's erythroblastic anemia was made on the basis of these clinical and laboratory findings.

The day following admission the temperature rose to 106° F. A transfusion of 150 c.c. of whole blood was given and the temperature rapidly returned to normal. The infant received seven transfusions during the first three months of his hospitalization and there were frequent and rapid variations in the size of the spleen. A surgical consultation was held with the pediatric staff and a splenectomy was decided upon. About fourteen weeks after admission, Jan. 26, 1942, when the spleen was considerably diminished in size, a splenectomy was performed under open drop ether. The operation was completed in forty-five minutes with very little loss of blood, and the patient was returned to the ward in good condition.

The spleen was enlarged and weighed 75 Gm. It was firm and enclosed in a smooth, glistening capsule. On section, the pulp presented a red, meaty appearance, and the splenic follicles were not visualized. The microscopic examination revealed the principal change to be in the Billroth's cords, which were considerably thickened due to fibrosis. In the splenic follicles, the germinal centers were conspicuously large and, in an occasional one, hemorrhage was present. The splenic sinuses were dilated and their lining cells swollen.

The postoperative course was uneventful. The child received elixir of feosol and two subsequent transfusions. The child was discharged to a convalescent home weighing 16 lb., 9½ oz., and with a blood count of 2.9 million red cells, 8.1 Gm. hemoglobin, and a color index of 0.98. The final smear showed normoblasts, erythroblasts, polychromasia, anisocytosis and poikilocytosis still present, and a platelet count of 638,330.

The child was readmitted on eight subsequent occasions. On each admission he received transfusions of citrated whole blood, and was returned in an improved condition to the convalescent home, where he received feosol and liver therapy.

The patient's final admission was on May 23, 1945. He was pale and poorly nourished and weighed 31 lb., 6 oz. The skull had prominent bilateral frontal bosses. The hair of the scalp was coarse and dry. The mongoloid characteristics of the face were accentuated by a small nose with a flat bridge. The heart appeared enlarged to both the right and left on percussion. The rhythm was regular but the sounds were of only fair quality, with a blowing systolic murmur over the entire precordium.

The lungs were clear to percussion and auscultation. The abdomen was distended, due to the enlarged liver, which was firm and nontender and extended two fingers below the umbilicus. The left upper quadrant scar of the splenectomy was well healed. The extremities were thin and spindly with cutaneous scars from the frequent transfusions.

The red blood count was 1.8 million and the hemoglobin 4 Gm. Successive counts ranged between 1.1 million and 2 million red cells and 4 to 5 Gm. hemoglobin. The hematocrit ranged from 14 to 16 mm. packed cell volume, the corrected sedimentation rate by the method of Wintrobe was 12 mm. per hour. The white blood count was 14,000, 54 per cent neutrophiles, 1 per cent myelocytes, 3 per cent metamylocytes I, 5 per cent metatmyelocytes II, 4 per cent eosinophiles, and 33 per cent lymphocytes. The platelets were 150,000 to 320,000 on this admission. A cell fragility test showed hemolysis to begin at 0.34 per cent and to be incomplete at 0.28 per cent, compared to a control that began at 0.44 per cent and was complete at 0.34 per cent.

The urine was positive in a 1:40 dilution and negative in a 1:80 dilution for urobilinogen, and positive directly for bile.

The x-rays of the skull at this time showed increase in thickness of the frontal bone and more pronounced fasiculation of the bony pattern. Examinations of the hands showed coarsening of the bony patterns, with osteoporosis and pronounced trabeculation.

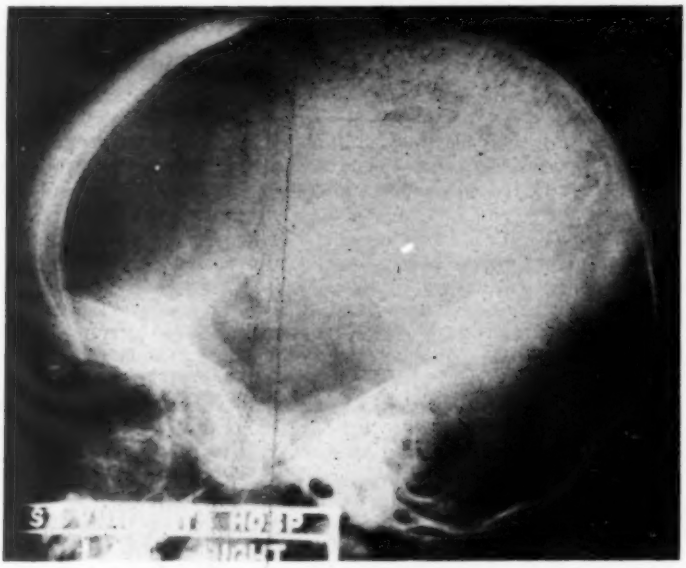

Fig. 1.—Case 1, K. L. Skull roentgenogram showing increase in thickness of frontal bone and fasiculation.

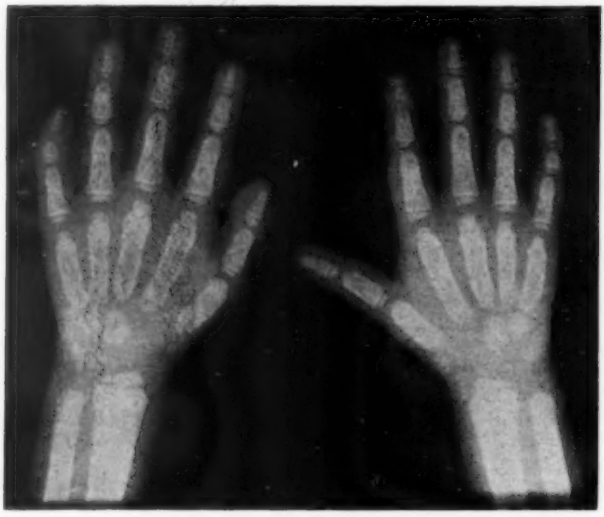

Fig. 2.—Case 1, K. L. Roentgenogram of hands showing cortical thinning and osteoporosis with increased trabeculation. Note squaring of ends of long bones.

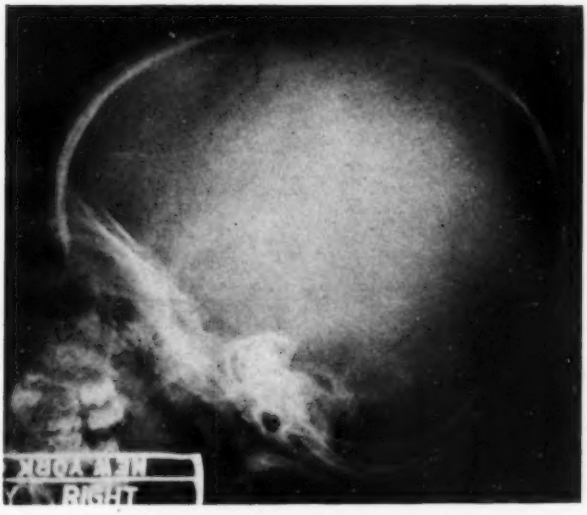

Fig. 3.—Case 2, P. M. Skull roentgenogram shows moderate thickening in frontal region and atrophy and mottling of the calvarium.

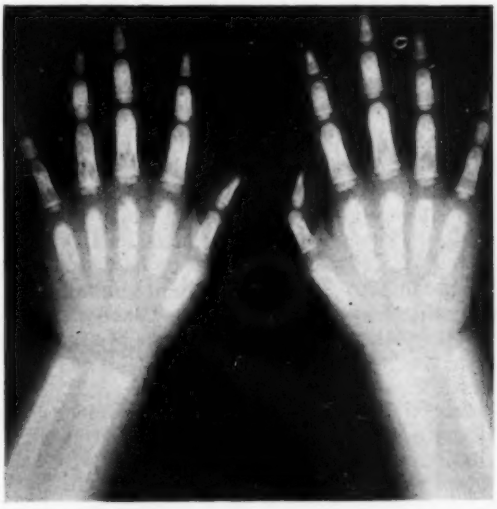

Fig. 4.—Case 2, P. M. Roentgenogram of hands showing cortical thinning and increased trabeculation of bony pattern.

The child had occasional episodes of fever, hyperpnea and lethargy, associated with epistaxis. There was poor response to transfusions and the patient's condition became progressively worse. He finally developed a generalized, puffy edema. There was a fever, the heart rate became very rapid and the heart sounds poor. The child died at the age of 4 years, 9 months. Permission for autopsy was refused.

A study of the blood of the patient's family is presented in Table I. None of them presented any symptoms of the anemia.

TABLE I. BLOOD STUDY OF FAMILY OF CASE 1

	FATHER	MOTHER	BOY 4 YEARS OLD	GIRL 6 YEARS OLD
Erythrocytes (in millions)	5.6	4.6	4.7	5.6
Gm. of hemoglobin	12.5	12.2	11.3	11.3
Target cells	moderate	moderate	few	few
Color index	0.76	0.90	0.82	0.68
Mean corpuscular volume	75 cu. μ	91 cu. μ	63 cu. μ	78 cu. μ
Hematocrit	42	42	30	44
Red cell fragility	Initial incomplete	Initial incomplete	Initial complete	Initial complete
Per cent saline	0.44 to 0.28	0.46 to 0.28	0.46 to 0.30	0.48 to 0.34

CASE 2.—P. M., a 3-year-old Chinese male infant, was admitted to St. Vincent's Hospital on Sept. 17, 1945. His parents first noticed a definite weakness and lack of activity when he was 7 months old. At that time, a local physician felt the child's spleen and advised hospitalization. The child was taken to another hospital where he received an investigation and periodic transfusions. There was no response to therapy and the parents took the child home for several months. He had occasional episodes of epistaxis, but there was no history of fevers or abdominal pain. Liver therapy and iron preparations had no effect on the blood picture or the child's symptoms. He was later taken to a second hospital and has been maintained by periodic transfusions until the present admission. The parents brought the child to this hospital in the hope that splenectomy would benefit him.

The child was born at home in New York City following a normal pregnancy. He was breast fed, and when weaned was put on an infant's diet of milk, cereal, and puréed vegetables. There was no history of childhood diseases, and no immunization. There were no known tuberculosis contacts, and the parents knew of no relatives who suffered from a disease similar to the patient's.

Both parents were born in China. The father had been living in the United States thirty years, and the mother, when the child was born, fifteen years. There are three siblings with no symptoms who are 17, 16, and 14 years of age.

On physical examination, the child appeared about the stated age and characteristically Chinese. His weight was 32 lb. There was an obvious pallor and the abdomen was slightly distended. The conjunctivae were pale, and there was a questionable icterus of the sclera. The pharynx was slightly injected and the mucous membranes were pale. The tonsils showed a moderate degree of hypertrophy but there was no cervical lymphadenopathy. The lungs were clear to auscultation and percussion, and the heart sounds were of good quality with no thrills or murmurs present. The abdomen appeared slightly distended, soft, and nontender. The spleen was palpable 7 cm. below the costal margin and very firm. The liver was 3½ cm. below the right costal margin, moderately firm, and nontender. The extremities were essentially negative except for pallid nail beds. The neurologic examination was noncontributory.

Roentgenograms of the skull showed moderate thickening of the bone in the frontal region as well as generalized atrophy and mottling of the bones of the calvarium. The x-ray of the chest showed the heart to measure 9 cm. in the transverse axis, which was slightly over normal, average for this sized thoracic cage. The lungs were moderately congested but showed no other pathology. Roentgenograms of the hands showed definite alteration of the bony structures. There was thinning of the cortex and coarsening of the lamellar pattern in all the metacarpals and phalanges.

The leucocyte count was 6,250 cells per cubic millimeter with 48 per cent neutrophiles, 5 per cent metamyelocytes I, 6 per ment metamyelocytes II, one per cent myelocytes, 3 per cent eosinophiles, 36 per cent lymphocytes, and one per cent monocytes. There were 2.65 million erythrocytes with a hemoglobin content of 9.4 Gm. There were 4 per cent erythroblasts, 2 per cent normoblasts, and one per cent Cabot's ring bodies per 100 white cells. Polychromasia and basophilic stippling were slight. There was moderate microcytosis, achromia, and anisocytosis, and slight poikilocytosis. There was no evidence of sickling of the erythrocytes. The serum bilirubin was 3.4 mg. per 100 c.c. The blood was type O, Kahn negative. A cell fragility test showed initial hemolysis beginning at 0.46 per cent concentration of saline and being complete at 0.32 per cent as compared with a control that began at 0.50 per cent and was complete at 0.40 per cent.

The analysis of the urine showed it to be normal.

The child was diagnosed as a case of Cooley's erythroblastic anemia. Splenectomy was not deemed advisable at this time and the child was discharged, to be maintained by periodic transfusions.

A hematologic study of the child's father, the only member of the family who would submit to the examination, showed 6 million erythrocytes with 16 Gm. hemoglobin. There was slight anisocytosis, polychromasia, and a few target cells. The mean corpuscular volume was 76 cubic micra, and the color index 0.8. The sickling preparation was negative. The reticulocytes were 1.6 per cent. The erythrocyte fragility test began hemolysis in 0.42 per cent saline and was complete in 0.34 per cent saline.

COMMENT

These cases illustrate further that Cooley's anemia is not limited to patients of Mediterranean origin.

The findings demonstrated by these two cases conform to the syndrome originally described by Cooley. There is a hemolytic, hypochromic anemia with erythroblastosis and a normal to decreased erythrocyte fragility. The roentgenograms of the long bones show the cortical thinning, and coarse medullary trabeculations characteristic in this disease. The bone changes in the first case were seen to become more and more pronounced while under observation. The skull, which was normal on admission, later showed increased thickening of the diploe and radial fasiculation. Neither case showed any response to hematinics or liver therapy.

The value of splenectomy in this disease is questionable. At present, it is doubtful if this operation alters the course of the disease, and the only indication for it is the discomfort caused by the increased size of the spleen. The target cells increased, following splenectomy, but these apparently are not a pathogenic factor.

As in Smith's series, hematologic investigation of these patients' families, in so far as their cooperation could be obtained, showed some evidence of the "trait" in the bloods examined. Target cells were present in all specimens, and

there was normal to diminished erythrocyte fragility. However, none of the relatives examined had any clinical signs of disease.

The writer wishes to acknowledge the assistance of the various members of the hospital staff in the presentation of this paper.

REFERENCES

1. Cooley, T. B., Witwer, E. R., and Lee, P.: Anemia in Children With Splenomegaly and Peculiar Changes in the Bones: Report of Cases, Am. J. Dis. Child. **34**: 347, 1927.
2. Smith, C. H.: Familial Blood Studies in Cases of Mediterranean (Cooley's) Anemia, Am. J. Dis. Child. **65**: 681, 1943.
3. Vorhees, N. W., and Sloan, F. R.: Mediterranean Anemia, J. A. M. A. **125**: 352, 1944.
4. Valentine, W. N., and Neel, J. V.: Hematological and Genetic Study of Transmission of Thalassemia, Arch. Int. Med. **74**: 185, 1944.
5. Cooley, T. B.: Presidential Address, Am. J. Dis. Child. **62**: 1, 1941.
6. Bywaters, E. G. L.: The Cooley Syndrome in an English Child, Arch. Dis. Childhood **13**: 173, 1938.
7. DhuyaGude, R. H.: Erythroblastic Anemia of Cooley in an Indian Boy, Am. J. Dis. Child. **67**: 290, 1944.
8. Dameshek, W.: Familial Mediterranean Target Cell Syndrome, Am. J. M. Sc. **205**: 643, 1943.
9. Foster, L. P.: Cooley's Syndrome (Erythroblastic Anemia) in a Chinese Child, Am. J. Dis. Child. **59**: 828, 1940.
10. Wang, C. Y., and Khoo, F. Y.: Hemolytic Anemia With Erythroblastemia, Chinese Med. J. **58**: 177, 1940.

HYPERSENSITIVITY TO PRIVINE

JACOB GREENBLATT, M.D.
STAMFORD, CONN.

AMONG the occasional reactions to privine* is a rare type of hypersensitivity peculiar to children, manifested chiefly by sedation and sometimes accompanied by mild collapse. This phenomenon has the characteristics of a true hypersensitivity in so far as it occurs following the recommended dose (one to two drops of 0.05 per cent privine in children). It also occurs following the accidental ingestion of much larger amounts of the medication; this cannot be classed as hypersensitivity, but the resulting syndrome is similar to reactions to therapeutic dosages in sensitive subjects. These two types of cases were decribed by Waring, and they are also the subject of the present report.

In 1945, Waring[1] reported three cases of sedation following the use of privine in children. One was a 3-month-old female, who was given two drops of 0.05 per cent privine in each nostril. On one occasion she slept eight hours, and on another occasion she slept twenty-four hours following medication. He also reports a 7-year-old girl, who was given five drops of 0.1 per cent privine in each nostril three times daily; she felt drowsy and talked vaguely for several hours subsequent to each treatment. The third patient was a 3-year-old girl, who drank about 8 c.c. of 0.05 per cent privine, and was drowsy for several hours. It is of interest to note that the first case had no reaction to the use of neosynephrine. Waring refers to Bonzanigo,[2] who found that ephedrine in large doses produces sedation in children between the ages of 3 months and 14 years.

Our first case is similar to the first one described above.

S. F. is a white male infant born Jan. 10, 1947, weighing 7 pounds, 1 ounce. Delivery was spontaneous; the mother's prenatal course was not unusual, and she was Rh-positive. Family history is negative for hypersensitivities except for a sibling, whose case is described in detail below. S. F. had an uneventful neonatal period, and made good progress on an evaporated milk formula and vitamins. On March 10, 1947, at the age of 2 months, he was given three drops of 0.05 per cent privine in each nostril for an attack of rhinitis. One-half hour later his mother noticed that he could not be aroused. He was examined shortly thereafter (by the author), and found to be pale and completely limp. Respirations were shallow; the rate was thirty times per minute. Several times per minute he would jerk his head to one side and gasp. Heart action was about 100 per minute. There was no fever; temperature varied between 98° F. and 99.2° F. (rectal). The baby could be aroused sufficiently to utter a faint cry when he was spanked; 0.2 c.c. of coramine was injected, and he was then hospitalized where inhalation of a mixture of 95 per cent oxygen and 5 per cent carbon dioxide was given, as well as 0.1 c.c. of epinephrine 1:1,000. At no time was he cyanotic however, and he was able to cry vigorously one-half hour after admission to the hospital. Still, he would lapse into a mild lethargy, and jerk his head and gasp intermittently. These signs gradually abated: three hours after admission he was able to take his formula, and after six hours all abnormal signs disappeared. X-ray of the chest did not reveal anything unusual about the heart or lungs. The blood study showed: red blood cells, 3,120,000; hemoglobin, 10.5

From the Stamford Hospital and the St. Joseph's Hospital, Stamford.

*Privine hydrochloride is a salt of 2 naphthyl-methyl-imidazoline dissolved in a medium containing phosphates, chloride, and dextrose. It is extensively used as a vasoconstrictor in rhinologic disorders, and is prepared in two concentrations: 0.1 per cent for adults and 0.05 per cent for children.

Gm.; white blood cells, 11,550; neutrophiles, 41 per cent; eosinophiles, 3 per cent; lymphocytes, 55 per cent; myelocytes, 1 per cent (8 per cent band forms) on admission. Before discharge on the next day, red blood cells, 3,520,000; hemoglobin 11 Gm.; white blood cells, 8,900; neutrophiles, 32 per cent; basophiles, 6 per cent; lymphocytes, 64 per cent; myelocytes, 4 per cent. He was given ferrous sulphate for his anemia and has remained well.

E. F., the late brother of S. F., was born on Oct. 26, 1944. Delivery was spontaneous, and it was noted that he had a cleft palate and lip, as well as a heart murmur and mongoloid features. He weighed 5 lb., 2 oz. at birth, gained very slowly, and was a feeding problem. At the age of 1½ months he developed a rhinitis for which he was given three drops of 0.05 per cent privine in each nostril. Soon thereafter his mother noticed that he became limp and hardly breathed. Examination did not reveal any other abnormalities; the lungs were perfectly clear, as in the preceding case. He was immediately hospitalized, given oxygen, and recovered in a short time. X-ray of his chest revealed moderate enlargement of the heart. Urinalysis was negative. Red blood cells were 4,230,000; hemoglobin, 85 per cent; white blood cells, 12,400; polymorphonuclears, 36 per cent; lymphocytes, 51 per cent; Myelocytes, 11 per cent (four normoblasts per 100 white blood cells). At the time, this case was not recognized to be one of privine sensitivity because of the presence of congenital defects. This baby subsequently succumbed to these defects at the age of 4 months. At autopsy he was found to have a patent foramen ovale, pulmonary edema, stenosis of the pulmonary valve, narrow pulmonary artery, hypertrophied right ventricle, and a cleft lip and palate.

Another local case, strictly speaking, not a hypersensitivity, has come to the author's attention.[3] A 14-month-old boy swallowed about 7.5 c.c. of 0.1 per cent privine. He slept for twelve hours and had a subnormal temperature. He was treated with caffeine and warmth, and made a complete recovery.

REFERENCES

1. Waring, J. I.: J. A. M. A. **129:** 129, 1945.
2. Bonzanigo, C.: Arch. f. Kinderh. **94:** 15, 1931.
3. Personal communication from Dr. Charles A. Murphy, Stamford, Conn.

The Social Aspects of Medicine

The interesting letter from Dr. Joseph Palma published in the July issue of the JOURNAL OF PEDIATRICS contained this statement: "The cornerstone of our great system of American medicine—the best that the world has yet produced under any system—is the maintenance of the sacred patient-and-doctor relationship." Of course, the patient-doctor relationship which exists in this country is not peculiar to this country in any way. It has existed since the time of Hippocrates the world over. Both Professor Lichtenstein and Professor Wallgren made it clear in their contributions to the Column* that the entrance of the State into the system of medical care in Sweden has not interfered one particle with the patient-doctor relationship. To my way of thinking there is nothing peculiar either about the "great system of American medicine." It is the system again which has been practiced in Europe since the time of Hippocrates and came to this country with its settlement. What interested me very much in Dr. Palma's statement was the implication that since the system of medical care in this country is the best in the world, it does not require change. The question is extraordinarily important to all of us, because if our system of medical care is adequate, such an investigation as the Academy is conducting is entirely needless.

So far as I know, there is no way of establishing, statistically or otherwise, the superiority of one system of medical care as compared to another. Certainly one cannot establish it from mortality statistics in which economic factors and standards of education and living are fully as much concerned as disease. Infant mortality, as a matter of fact, is lower in several countries than in the United States. My personal belief is that the medical care in the Scandinavian countries is far and away superior to the medical care in the United States, but this is entirely a personal view. Certainly in the Scandinavian countries not only is general practitioner service available, but specialist service is available to every citizen, as is brought out by Professors Lichtenstein and Wallgren. In this country even general practitioner service is not to be had by all the population and the service of specialists is at the command of only the well-to-do and those of the middle and lower economic groups near large medical centers.

The question raised by Dr. Palma is so important that I asked him if he would be kind enough to write a special communication to the JOURNAL, giving in detail his point of view. At the same time I wrote to Dr. James Wilson and to Dr. Allan Butler for their views in regard to the adequacy of medical care in this country. The replies of Dr. Wilson and Dr. Palma follow.

E. A. P.

Dear Dr. Park:

A short time ago I prepared a statement on the social aspects of medicine, a copy of which was sent to the editor of the JOURNAL OF PEDIATRICS, the various state chairmen of the American Academy of Pediatrics, and to many of my friends throughout the country. You have courteously extended to me the opportunity of writing further on this subject for the column appearing in the

*Lichtenstein, A.: J. PEDIAT. 28: 503, 1946.
Wallgren, A.: J. PEDIAT. 30: 361, 1947.

JOURNAL, "showing why the American system is the best that the world has yet produced and your opinion whether or not medical care in the United States is adequate as it is."

It is not my intention to yield very far from my original statement that "any attempt to answer in detail or point by point the specious arguments advanced by . . . , the professional do-gooder's and fellow travelers is a mistake and a waste of time," as the "yes, it is, no, it isn't" type of argument leads only to acrimony and confusion. However, I shall attempt to explain further my views on the subject.

It takes a little pride in what is right with American medicine to state that it is the best that the world has yet produced under any system, without recourse to the statistics on morbidity and mortality and other recitations on the best features of American medicine.

The two main points around which the proponents of government in medicine center all their arguments are that (1) the cost of medical care is too high and (2) medical services are not adequately distributed. These defects are admittedly problems that must be met, but I submit that government in medicine will not solve them except at the sacrifice of personal freedom and private enterprise. The first Wagner-Murray-Dingell Bill (S. 1606-HR 4730) estimated that the cost of rendering governmental medical care would approximate four billion dollars annually and proposed that this sum be raised by a compulsory sickness tax of 4 per cent on the income of both employed persons and self-employed individuals up to $3,600 a year. The new bill, the so-called Wagner-Murray-Dingell-Pepper Bill (S. 1320) estimates the cost as approximately five billion a year, a very sizeable increase in the cost, even before the bill has been enacted and put into force. This increased approximate cost would necessarily increase the compulsory sickness tax to 5 per cent of income. Experience in European countries has shown, for those who will take the time to look at the records, that costs continue to increase with corresponding lowering of the quality of medical care in government-controlled schemes of medical care, and I am in agreement with those informed persons in this country who believe that the total annual cost of social and medical insurance in the United States will ultimately take about 25 per cent of the national income.

There are two basic reasons why the cost of a compulsory, Federally administrated system of medical care cannot be maintained at a stationary level over a long period of time. The first is the human factor. Individuals, both recipients and participants—at least a certain percentage of these individuals—will take every advantage of the system whether the sickness is real or imagined. The second basic reason is the political aspect of the administration of medical care. The popular, vote-getting appeal of broader coverage at less cost naturally is great, and politicians, likewise human beings, would not seriously oppose the popular demand for such liberalization. The greater tax burden necessary to implement the liberalization would, of course, have to be skillfully hidden.

The second defect in the problem of medical care—that of inadequate distribution—is again not solved by government-controlled medicine, except by the device of compulsion and regimentation of the members of the profession and of recipients of services. The new bill (S. 1320) makes a few changes in the administration of the national health insurance fund but still reads: "All functions of the Board shall be administered by the Board under the direction and supervision of the Federal Security Administrator." Other concessions have been made toward decentralization and toward the maintenance of the confidential nature of reports and the preservation of the doctor-patient relation-

ship, but in the ultimate analysis the simple fact remains that the independent status of the physician and the profession will be sacrificed and that we will be taking care of our patients by directives and other orders from the Federal Security Administrator, who will be a lay individual. Those of us who had any considerable time under military medicine—an acknowledged necessity for the purpose of winning the war—have had enough of medicine by directives. We know that private enterprise and a free profession can do it better.

Application of the insurance principle offers a solution to the problem of the unequal distribution of the burdensome costs of medical care. The voluntary agencies already functioning in many states give promise of success, although many difficulties remain to be worked out. But no one should be misled into believing that the proposed Bill S. 1320 or any similar legislation is a sound application of the insurance principle.

All that is needed is further opportunity under our democratic system of free enterprise for the alert medical profession to continue its efforts to solve the admittedly two great problems—the increase in cost of medical care and the adequate distribution of medical service.

Finally, then, the solution of these problems is simply one of your individual philosophy. If you believe that the state is the master of the people or that progress can be made only by the state continuing to take unto itself increasing powers over the individual citizen and his freedom, if you believe that the best interests of all the people are better served by planning from the top, then you are for state medicine and the inevitable further traveling along the road to statism, collectivism, or whatever name you want to call it.

However, if you believe that the maintenance of health is the moral obligation of the individual; if you believe that to yield on even one small point of a principle is to lose all freedom eventually; if you believe that, under the democratic free enterprise system, America has created the greatest system of medical care yet produced under any system of government, and that we can continue to solve the problems of what is wrong with that system in the future as well as we have in the past; then you are definitely opposed to further extension of government in medicine.

Several answers to my original statement have expressed again the attitude that "It can't happen here." As an active participant in the tragic events of that memorable day, Dec. 7, 1941, I most vigorously oppose this point of view. There must not be a second Pearl Harbor.

JOSEPH PALMA, M.D., F.A.A.P.

Dear Dr. Park:

If progress is to be made in plans for the improvement of child health, discussion among physicians must always be objective, unemotional, and, when possible, factual. The opportunity that this column presents for a free exchange of opinion in open letters may assist in such objective thinking.

Reading the letter of Dr. Joseph Palma of Hawaii, I became concerned with an attitude of self-satisfaction and rather priestlike superiority that doctors too commonly assume to support their beliefs in medical-economic matters. Such attitudes are very unpersuasive to many lay people. Doctor Palma is bitterly opposed to what he calls "compulsory prepayment medical care." Many others, including myself, are frightened, as is he, by the possibility of grave and perhaps irreversible errors that may result from our government's rather naïve attempts to purchase good medical care wholesale for our people. In combatting what we

think are foolish and poorly conceived attempts to too rapidly "improve" medicine, we must, however, be cautious that we ourselves are honest and realistic about our own profession and do not resort to specious phrases and shibboleths.

This letter is to object to one particular sentence in Doctor Palma's letter, "The cornerstone of our great system of American medicine, the best that the world has yet produced under any system, is the maintenance of the sacred doctor-patient relationship." Relative to other countries, I am sure that our system of medicine in this country is excellent. I do think, however, that it could be questioned whether it is best in *all ways,* and yet I see no possible way of proving this, since certainly the only data available, morbidity and mortality figures, would not have a direct bearing on the question. However, is the question the least bit important? Should not the real question be, is our system as good as it can be or as good as it ought to be, and can any changes be made that will further improve it? Why should we worry whether it is better than any other country's? Our automobiles are better, and our plumbing is better, but we still think something can be done to improve them.

If we asked many a common citizen of this country whether he feels that the medical attention he gets or can get is satisfactory, there would be no question about the pessimism of his answer. As physicians, we certainly feel that oftentimes his dissatisfaction is with the fundamental inadequacy of medical knowledge and not actually with its application, but, nevertheless, the common man expresses an opinion to which we must pay a great deal of attention, and he represents a great many votes. Many in our country do not feel that the medical attention they are getting is qualitatively satisfactory, and most do not feel that it is quantitatively satisfactory. We, ourselves, therefore, should be concerned about this critical attitude of the public and try to do something about it, rather than simply to reiterate that we are giving the best medical attention the world has produced. Anyone who has had an opportunity to critically evaluate the results of medical care as it is carried out on infants and children cannot help but be certain that far less than the best medical care that could now be given is actually being practiced. A great majority of physicians who are caring for children in this country have had less than one month's formal training in pediatrics. Many have had none at all. Although it is an ideal which will take a long time to reach, it is too much to ask that our children should be cared for by a physician who has had as much training as the minimum required by the American Board of Pediatrics, or are the advantages of such competence to be restricted to "upper classes"? We can say, certainly, that the practice of medicine with children is not as good as it might be if doctors were better trained and if there were more of them, and that we as physicians would not want our own offspring cared for by the majority of physicians in practice.

Let us look at the phrase "sacred doctor-patient relationship." This sounds a bit like something out of a city ward Fourth of July oration. To many it will seem a bit sanctimonious and hypocritical to use the word "sacred" about such medical matters. The family doctor who becomes the self-sacrificing and patient confidante, always on call to enter the whole economic, physical, and moral problems of the family, maintains a relationship very precious and valuable, and for which perhaps the word "sacred" might be used. Though many patients have the finest relationship with their doctors, we should ask ourselves whether any action of our government or any action of the American Medical Association can destroy or produce a good doctor-patient relationship. Isn't this something that the doctor himself in any circumstance must bring about? I cannot help but recall the instances where parents of children in a busy pediatric out-patient department, not knowing who was who among the

many white-coated men they saw, have insisted on being seen on a second visit by the same intern and have resented and refused the attentions of anyone else, including the chief of service. There we have a patient-doctor relationship which may not be sacred but is, nevertheless, good. The intern, even under the bad circumstances in a city hospital out-patient clinic can develop a doctor-patient relationship that is admirable. This relationship is surely a matter of personalities, of patience, and of kindness, not of buildings or organizations or governmental edicts. It is a pity that this phrase needs to be battered around for political purposes. I think we had better ask ourselves whether any doctor-patient relationship which must be maintained in the office of a physician who can spend not more than ten minutes for each patient is precious enough to be preserved at all costs. I certainly think that the most sacred aspect of a doctor-patient relationship is not likely to be well developed under the pressure of modern practice, and yet this is the circumstance that exists in a great many pediatricians' offices under the freest system which we ourselves can construct.

I firmly believe that the medical care in this country as given to the average patient would be much worse under the effects of such an omnibus of vaguely planned uplift that we see in the Wagner bill. I sincerely hope that our people's intense desire for more and more medical services, exploited by the inevitable tendency of government officials and public health men to increase their administrative authority, does not lead to premature and irreversible federal action that will at best improve the quantity at the cost of quality in service, but the way to prevent any ill-conceived government action is to improve our own organization and activities and not to rest contented with repeated dogmatic assertions of our own excellence.

(Signed) JAMES L. WILSON, M.D.

Ann Arbor, Mich.

I have just received a copy of the testimony submitted on behalf of the American Public Health Association on Senate Bill 545, by Reginald M. Atwater, M.D., Executive Secretary. Since parts of it are pertinent to the question whether medical care in this country is adequate at the present time, I have obtained Dr. Atwater's permission to publish them. I do not publish the entire statement of Dr. Atwater because the remainder relates to the Taft Bill and I hope to present a complete critical review of this later. The relevant parts of Dr. Atwater's "testimony" follow: E. A. P.

TESTIMONY ON BEHALF OF THE AMERICAN PUBLIC HEALTH ASSOCIATION ON SENATE BILL 545

R. M. ATWATER, M.D.

"A large portion of the population receives insufficient and inadequate medical care, chiefly because persons are unable to pay the costs of services on an individual payment basis when they are needed, or because the services are not available."* Numerous studies have documented the truth of this observation. The Committee on the Costs of Medical Care, which was headed by Dr. Ray Lyman Wilbur, found in 1928-31 that the lack of adequate medical care was not confined to the very lowest income groups but extended throughout all or most of the population. While professional standards called for approximately 5½ physician's calls per person per year, only those with an income of $10,000 or more attained this standard. Persons in families with incomes between

*Medical care in a National Health Program adopted at the 1944 Annual Meeting of the A. P. H. A.

$5,000 and $10,000 had 4 physician calls per person; between $3,000 and $5,000, only 3 physician calls; and below $3,000, only 2 to 2½ physician calls. Similar inadequacies were discovered in regard to general hospital care, dental care, immunizations, laboratory services, and refractions and glasses.[1]

Studies made in 1941 indicate some of the economic factors responsible for these inadequacies. In that year, families and single consumers with an income of $5,000 and over spent an average of $310 for medical care; those with incomes of $3,000-$5,000 spent $151; the $2,000-$3,000 income group spent $105; and those with incomes below $2,000 spent an average of $53 for medical care.[2]

How Many Americans Can Afford Medical Care?

In 1939, the Bureau of Medical Economics of the American Medical Association reached the conclusion that families with incomes of less than $3,000 sometimes require outside assistance in the case of major illness, while those with incomes below $1500 may need special assistance even for minor illnesses.[3] These data gain added significance when it is recalled that even in 1941, when the per capita income reached its highest pre-war peak, 51 per cent of American families and single consumers had annual incomes of less than $1500, and 85 per cent had annual incomes below $3,000.[2]

Do Most Americans Receive Adequate Medical Care?

It is true that there has been a substantial increase in money incomes during the war years. Nevertheless, the Federal Reserve Board reported that in 1945, at the peak of wartime prosperity, 47 per cent of all families and single consumers had total annual incomes of less than $2,000, 70 per cent had incomes of less than $3,000, and 92 per cent had incomes of less than $5,000.[4] Moreover, there has been a very substantial increase in the cost of living and the tax burden, so that real incomes have not changed nearly as much as the statistics for money incomes would appear to indicate. In addition, the costs of medical care have risen considerably, both because of scientific developments which have continued to make adequate medical care more expensive, and the general rise in costs of services which has increased the cost of hospital care, for example, to unprecedented heights. We may therefore conclude that the statement that a majority of the population does not receive adequate medical care is certainly as true today as it was before the war.

Medical Costs Are Uneven and Unpredictable

A major reason that inability to pay for medical care is not limited to the very lowest income groups lies in the uneven distribution of medical costs. In 1941, for example, among farm families with annual incomes of $750 to $1,000, 37 per cent spent less than $25 for medical care, while 18 per cent of the families spent anywhere from $100 to $500.[5] This uneven distribution holds true for all income groups. It is no comfort to the individual family to know that the *average* cost of medical care is 4 per cent of income. If a family with an annual income of $3,000 lays aside 4 per cent or $120 for medical costs, it may spend $10 or it may have to spend $1,000. To the individual family, medical costs are entirely unpredictable and often cause a crushing financial burden. There

[1] Medical Care for the American People—Committee on the Costs of Medical Care, No. 28, University of Chicago Press, 1932, p. 8.

[2] (Spending and Saving of the Nation's Families in Wartime) U. S. Dept. of Labor, Bull. No. 723, 1942, p. 2, p. 18.

[3] Factual Data on Medical Economics, Bureau of Medical Economics, American Medical Association, Chicago, 1939, p. 66.

[4] (*Federal Reserve Bulletin*, August 1946, p. 851).

[5] *What Farm Families Spend for Medical Care*, U. S. Dept. of Agr. Misc. Publ. No. 561, April 1945, p. 9.

are few of us indeed who from personal resources can meet the medical costs of a disease such as cancer, or of a serious accident, with care lasting over a period of months and requiring the services of skilled specialists. That is why a national program of medical care must be oriented towards meetings the needs of the entire population, not merely the very low income groups. It is essential also that the program does not result in two separate systems of medical care, one for the poor and another for the well-to-do. for these reasons our Association declared that "A national program for medical care should make available to the entire population all essential preventive, diagnostic, and curative services."

News and Notes

The **American Board of Pediatrics** will hold Fall examinations on Dec. 5, 6, and 7, 1947, at Dallas, Texas, and on Jan. 9, 10, and 11, 1948, at Philadelphia, Pa. For further information write The Secretary, 718 Royal Union Bldg., Des Moines, Iowa.

The American College of Physicians announces that a limited number of **Fellowships in Medicine** will be available from July 1, 1948 to June 30, 1949. These Fellowships are designed to provide an opportunity for research training either in the basic medical sciences or in the application of these sciences to clinical investigation. They are for the benefit of physicians who are in the early stages of their preparation for a teaching and investigative career in Internal Medicine. Assurance must be provided that the applicant will be acceptable in the laboratory or clinic of his choice and that he will be provided with the facilities necessary for the proper pursuit of his work.

The stipend will be from $2,200 to $3,000.

Application forms will be supplied on request to The American College of Physicians, 4200 Pine Street, Philadelphia 4, Pa., and must be submitted in duplicate not later than November 1, 1947. Announcement of the awards will be made as promptly as is possible.

The following pediatricians have been certified in the subspecialty of Allergy.

Dr. William Potter Buffum, 122 Waterman Street, Providence 6, Rhode Island
Dr. Joseph Harman Fries, 25 Plaza Street, Brooklyn 17, New York
Dr. Jerome Glaser, 300 South Goodman Street, Rochester 7, New York
Dr. John E. Gundy, 264 King Street, Port Chester, New York
Dr. Lewis Webb Hill, 319 Longwood Avenue, Boston, Massachusetts
Dr. Arthur J. Horesh, 10515 Carnegie Avenue, Cleveland 6, Ohio
Dr. Arthur Paul Keller, 423 Market Street, McKeesport, Pennsylvania
Dr. Morris Y. Krosnick, 257 Church Street, New Haven, Connecticut
Dr. Samuel J. Levin, 469 Fisher Building, Detroit 2, Michigan
Dr. W. Ambrose McGee, 1601 Monument Avenue, Richmond 20, Virginia
Dr. William Panitch, 90 Baldwin Avenue, Newark, New Jersey
Dr. Bret Ratner, 50 East 78th Street, New York City, New York
Dr. Orlindo L. Ross, 9 Exchange Place, Salt Lake City, Utah
Dr. Oscar M. Schloss, 125 East 72nd Street, New York City, New York
Dr. Hyman A. Slesinger, Windber Hospital, Windber, Pennsylvania
Dr. Joseph Weiner, 100 Whitney Avenue, New Haven, Connecticut
Dr. Benjamin Zohn, 1449 Union Street, Brooklyn 13, New York

Book Reviews

Medicine in the Changing Order: Report of the New York Academy of Medicine Committee on Medicine and the Changing Order. New York, 1947, The Commonwealth Fund, 240 pages.

In December of 1942 the Council of the New York Academy of Medicine authorized the appointment of a group to study the complex problems of medical care. Under the Chairmanship of Dr. Malcolm Goodridge, with Dr. Iago Galdston as secretary, a committee of fifty was organized containing thirty-three physicians, many of whom are of national eminence, and seventeen social and civic leaders including representatives of the dental and nursing professions. The full committee and its planning and reviewing groups held 120 meetings in the course of its three-year study. Over fifty men and women were invited and appeared before the committee, representing all of the related fields of medical care as well as all shades of economic and social thought. In addition, the committee fostered a number of studies, some of which have been reviewed previously in the JOURNAL.*

The work of the committee was financed by grants from the Millbank Fund, the Josiah Macy Junior Foundation, and the Commonwealth Fund. The original resolution of the Academy Council was to the effect that a committee be appointed "with unlimited latitude to study present trends in medicine." The committee defined its objectives as follows: "To be informed on the nature, quality, and direction of the economic and social changes that are taking place now and that are clearly forecast for the immediate future; to define in particular how these changes are likely to affect medicine in its various aspects; to determine how the best elements in the science of medicine and in its services to the public may be preserved and embodied in whatever new social order may ultimately develop."

The reviewer has gone into detail as to the origin, purposes, and work of the committee, since this final report, the result of an unbiased, thorough study, will beyond question have a decided influence on medical thought and practice, and in charting the course for changes in medical care in the near future.

In its first chapter on the "Origins of the Present Problems," the report discusses from a historical standpoint the development of medicine as a science, the rise and impact of preventive medicine, the growth of hospitals, and the progress in medical education. This development of medicine as a science led to the present economic problems of medical practice. "But as medicine and surgery progressed the whole situation changed. . . . The mounting costs of medical practice confront the public in the shape of fees charged by physicians, hospitals, laboratories, and the like. But the origins of the costs are essentially those very precise, involved, and expert procedures which make modern medicine so

*Government in Public Health. H. S. Mustard, **30**: 533, 1946. Medical Education and the Changing Order. B. Allen, **29**: 535, 1946.
American Medical Practice in Perspectives of a Century. B. J. Stern, **29**: 534, 1946.
A Future for Preventive Medicine. E. J. Stieglitz, **29**: 534, 1946.

widely desirable and effective. The problem of how to reduce the one and retain the other, how to make medical care widely available without losing its effective qualities, is the core of the current problem in medicine. As this problem emerged after about 1915, the form it assumed and the solutions suggested naturally took their pattern from changing situations and social attitudes.'' All this has been stated before, but never any better or more concise than in the above quotations. So many fail to realize that much of the current debate over medical problems is in reality a debate over differing social ideologies, in which medicine offers a convenient focal point for discussion.

In the following chapters on ''Medicine in Recent Decades'' and ''The Health of the Nation,'' the emergence of insurance as a factor in meeting and spreading costs and the status of the nation's health is described. The report finds that neither the contention of some that we are the healthiest nation in the world, nor the mortality statistics which prove that the United States ranks seventh among the nations with the lowest death rates, is meaningful under close scrutiny. As for the problem of medical services, ''far too much emphasis'' has been placed ''upon the purely economic aspects. . . . While income factors are very important, exclusive and excessive emphasis on this tends to distort the problem. . . . For example, it is often said that the great trouble is simply inability to pay medical bills, and that if arrangements were only made to meet these, other problems would perforce be resolved. Actually, such an arrangement would very likely perpetuate poor standards of practice and probably extend them.'' This last quotation expresses the thinking of many of the pediatricians whose chief interest for years has been better medical care for the children of America in opposing the E. M. I. C. program and the Pepper bill fostered and promulgated by the Children's Bureau.

The next subjects considered in the report are medical care in urban and in rural areas, the latter being gone into in much detail. Chapter VI discusses the extension of the public health services. In one section of this chapter the inadequacies, needs, and financing of local health services are considered, and in another those of the federal and state health services.

Throughout the report, distinction between mere quantity and the quality of medical services is emphasized. In this respect the report differs from that of the majority report of the Committee on the Costs of Medical Care, which appeared in 1932, although in many of the final findings the two reports are in agreement. Most of the discussion in recent years has so centered upon the economic and social aspects, that the problems of the quality of medical care which are fundamental to better medical services have largely been ignored. The small Committee for the Improvement of Medical Care has been one of the few groups which has consistently stressed this aspect of the problem in its reports. It is for this reason that the three chapters, ''The Quality of Medical Care,'' ''Preventive Medicine,'' and ''The Hospitals,'' which comprise about a third of the Academy Committee report, are so important in making it, as a whole, so comprehensive.

The committee finds that the provision of adequate medical care calls for many changes in medical education and practice. In medical education it must go back as far as the high school. Certain changes in the medical school program should be made in keeping with the development of scientific techniques, and the emphasis in instruction should be changed in part from the treatment of disease to prevention. The internship should be closely integrated with the medical school program. Medical practice to meet modern demands and utilize modern methods should be reorganized along lines of group practice, whose advantages and difficulties are considered in detail. Preventive medicine, defined as that which the physician furnishes the individual as contrasted with the public health medicine, which deals with large social groups, must be accentuated in medical education and developed in medical practice, if medical care is to be adequate to the individual.

The hospital, which has undergone such a complete transformation in recent years, is very thoroughly discussed from the technical, organization, and financial sides, and some twenty-two recommendations as to the hospital are made by the committee. The need

for rural hospitals to furnish technical facilities is recognized. The importance of O.P.D. extension and of the hospital as a nucleus for group practices is stressed.

In Chapter XI the report takes up the question of medical insurance as a specific topic, although it is referred to many times in previous sections of the report. The discussion is thorough and fair and we quote some of the findings. "The problems which compulsory national medical insurance engenders appear so formidable, and the evils it threatens so plain, that the committee strongly advises against hasty action. Once the country commits itself to this type of policy and legislation it cannot retrace its steps. . . . The Committee believes that medical insurance is one of the essential requirements in solving the problem of medical care distribution. It agrees that compulsion by government would accelerate the extension of insurance to all the people. It agrees, also, that voluntary insurance will spread only slowly and incompletely among the low-income families. It is at the same time convinced that voluntary insurance provides flexibility for local initiative and is designed to encourage new and better methods of organized medical services, such as group medical practice, within the physical and personnel limitations of each area . . . everything should be done, by way of grants, subsidies, and employers' contributions to hasten the growth of voluntary medical insurance." This last implies that tax money grants should be made to voluntary insurance schemes to furnish medical care for those with an income too low to participate on an independent basis. Coverage should also be extended to higher income groups to spread the risk by increased coverage. The same medical service naturally would be furnished to all participants.

In the final chapter (XII), "The Method and the Goal," the committee makes a comprehensive statement of its views and findings, some of which have been discussed above. The Committee is in agreement on many points. Medical service should provide all that science can offer, and its benefits should be available to all. Medical service at present is not optimally organized, and plans for its improvement should be based on study and not directed to the support of preconceived schemes not based on such study. No one plan can be applicable to all people of our country, and hence experiments are needed. While the general public has a vital interest in plans for changes, the physicians should have a dominant rôle in the preparation of plans which they will be called upon to carry out. Gradual improvement and extension are preferable to revolutionary changes. While government has a direct responsibility, rapid and sweeping changes brought about by legislation would defeat their own purposes by impairing the spirit and quality of medical care.

Surely there is no thinking person who is interested in better medical care who cannot be in agreement with the committee in these findings. They doubtless will be unsatisfactory to those who believe in a totalitarian system of government, whether they be fascists or communists.

Specific formulations are as follows:

"In extending medical service and perfecting its organization, quality must be preserved.

"Provision of public health services is a prime essential.

"Improvement in medical service requires effective use of hospitals with adequate facilities.

"Success will require trained professional and nonprofessional personnel.

"For optimal results, organization and cooperation of physicians are required. [Group practice.]

"In the improvement of medical services, voluntary prepayment plans are needed.

"The goal should be comprehensive medical service. [Health supervision and preventive as well as curative treatment.]

"Extensive education for both physicians and the public will be required.

"Progress in the extension of medical service must be varied and adapted in each instance to the needs of the community.

"Government aid will be required." (Local, State, or Federal, or a combination, for the extension of hospital and health facilities, and aid to voluntary prepayment plans during the formative period.)

As a whole the report is one of the sanest and most comprehensive discussions that has been made on the problems of medical care. Parts will be unpleasant reading to the proponents of the *status quo*, while the radical element will be disappointed by its opposition to compulsory insurance. We hope the Commonwealth Fund which publishes the report, or some other source, will place the book on the shelves of every hospital and medical library, as well as our public libraries, so that it will have the influence it deserves on the thinking of those struggling in the complex problem of medical care.

B. S. V.

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